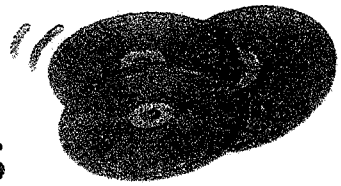
Registration Number 83399-16



NEW APPLICATIONS

DATE: APR 17 2015

FILE REG NUMBER: 83399-RA

FEP (OPPIN ENTRY): LV APR 20 2015

(Initial & Date)

FILE ROOM: _____

(Initial & Date)

SIG: _____

(Initial & Date)

FILE ROOM: _____

(Initial & Date)

ASSIGN TO PM: AD____ **RD** ✓ **BPPD**_____

_____ **JACKET TO SHELF (DATA)**

REVISED 11/28/12

PROCESSING REQUEST

Reg # 83399-16 **Decision #** 503583

Description: New product registration

Electronic Label & Letter (see PPLS):	**OR**	**Non Electronic Label & Letter** (Scanning required):
☒ Dated: 2-8-2016		☐ Dated:

Only one label type should be selected

Other Materials Sent (see jacket):

☒ New CSF(s) Dated: 2-4-2016

☐ Other:

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Rita Kumar

Division: RD

Phone: 703-308-8291 **Date:** 2-25-16

Kumar, Rita

From: Kumar, Rita
Sent: Thursday, February 11, 2016 11:57 AM
To: Alicia Henk
Cc: 'Katy Hernandez'
Subject: Pending application for 83399-RA, cat spot-on
Attachments: 83399-16-20160208.pdf

Dear Alicia: Please see attached. This action is now complete. Kindly acknowledge receipt.
Regards,
Rita

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Registration Division (7505P)
1200 Pennsylvania Ave., N.W.
Washington, D.C. 20460

NOTICE OF PESTICIDE:
_X_ Registration
___ Reregistration

(under FIFRA, as amended)

EPA Reg. Number:	Date of Issuance:
83399-16	2/8/16

Term of Issuance:
Conditional, Time-Limited
Expires: 2/8/2018

Name of Pesticide Product:
Imidacloprid and Pyriproxyfen Spot-On Solution for Cats

Name and Address of Registrant (include ZIP Code):

Alicia Henk
Director, Development and regulatory Affairs
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Registration Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is conditionally registered in accordance with FIFRA section 3(c)(7)(A). You must comply with the following conditions:

1. Submit and/or cite all data required for registration/reregistration/registration review of your product under FIFRA when the Agency requires all registrants of similar products to submit such data.

Signature of Approving Official:	Date:
Venus Eagle, Product Manager 01 Invertebrate-Vertebrate Branch 3, Registration Division (7505P)	2/08/16

EPA Form 8570-6

2. This registration is time-limited and expires 2/8/2018.

3. You must submit quarterly enhanced incident reports and quarterly sales information in doses sold for this product beginning within 3 months of the date the product is first released for shipment, on the first day of the quarter (i.e., January 1, April 1, July 1, or October 1). Please flag any Confidential Business Information as such. Submit enhanced incident reporting and quarterly sales information to the Product Manager's attention. The following is a list of information that must be included in the quarterly reports for each incident:

    - EPA Registration Number
    - Product name (brand name)
    - Lot #
    - Where purchased: internet, store, veterinarian
    - Active Ingredient(s)
    - Weight range for product
    - Date on which incident occurred. (mm/dd/yyyy)
    - State in which the incident occurred. (standard 2 letter abbreviation)
    - Registrant case #
    - Species: dog, cat, other (specify)
    - Breed: (as reported by pet owner)
    - Age: months or years
    - Sex: M, F, or neutered
    - Weight: pounds
    - Primary Route of Exposure: dermal, oral, other animal, inhalation, other
    - Body System: neurological, dermatological, GI, respiratory, ocular, other
    - Major signs noted with separate column for each sign, using standard terminology
    - Time to Onset: (hours, days)
    - Treated by veterinarian: yes or no
    - First time product used: yes or no
    - Misuse: use on incorrect species, overdose, too frequent dosing, other (describe)
    - Any known precondition
    - EPA Severity Code: death, major, moderate, minor
    - Outcome: died, recovered, still treated, unknown

4. Along with the enhanced incident reporting, you must submit an analysis of the incidents seen, to include the following details:

    - All incidents should be reported including all minor dermal and ocular irritation reports.
    - Summary table for cats showing number of incidents of each severity code for each route of exposure. Each incident should only be reported once. If one incident has several routes of exposure, the order should be ocular > oral > dermal. In other words, an incident with both oral and dermal exposure would be reported as oral exposure, and an incident with both ocular and oral exposure would be reported as ocular exposure.

- A similar summary table for dogs (misuse or secondary exposure) showing number of incidents of each severity code for each route of exposure.
- Summary table for dogs and table for cats showing number of incidents that are believed due to secondary exposure (e.g., multi-pet households).
- A summary table for cats showing number of incidents for each severity code for these age ranges: <3 months, 3-6 months, 6-9 months, 9-12 months, 1 yr, 2 yr, 3 yr, 4 yr, 5 yr, 6 yr, 7 yr, 8 yr, 9 yr, 10 yr, 11 yr, 12 yr, 13 yr, 14 yr, 15 yr, >15 yr.
- A summary table showing the number of cat incidents for each severity code for each pet weight range on the product label, as applicable.
- A summary table for cat weight showing number of incidents for each product weight range. This table should show number of incidents in cats weighing less than that product weight range, number of incidents in cats in lower half of weight range, number of incidents in cats in upper half of weight range, and cats weighing more than the product weight range, as applicable.
- Table showing number of incidents for each cat breed, where provided.
- Table showing number of incidents in cats for each clinical sign.
- Table showing number of incidents in cats for each organ system.
- Report aggregate incidents, but do not combine moderate and minor incidents.

If EPA determines that future mitigation measures are necessary for all pet spot-ons, the Agency will inform registrants. If mitigation measures are necessary, EPA may take regulatory action.

5. You are required to comply with the data requirements described in the DCI and EDSP Orders identified below:

   Imidacloprid GDCI-129099-951
   Pyriproxyfen GDCI-129032-1299
   Imidacloprid EDSP-129099
   Pyriproxyfen EDSP-129032

   You must comply with all of the data requirements within the established deadlines. If you have questions about the Generic DCI or EDSP Order listed above, you may contact the Chemical Review Manager in the Pesticide Reevaluation Division:
   http://www.epa.gov/oppsrrd1/contacts_prd.htm

6. The data requirements for storage stability and corrosion characteristics (Guidelines 830.6317 and 830.6320) are not satisfied. A one year study is required to satisfy these data requirements. You have 18 months from the date of registration to provide these data.

7. Make the following label changes before you release the product for shipment:

   - Revise the EPA Registration Number to read, "EPA Reg. No. 83399-16."

8. Submit one copy of the final printed label for the record before you release the product for shipment.

Should you wish to add/retain a reference to the company's website on your label, then please be aware that the website becomes labeling under the Federal Insecticide Fungicide and Rodenticide Act and is subject to review by the Agency. If the website is false or misleading, the product would be misbranded and unlawful to sell or distribute under FIFRA section 12(a)(1)(E). 40 CFR 156.10(a)(5) list examples of statements EPA may consider false or misleading. In addition, regardless of whether a website is referenced on your product's label, claims made on the website may not substantially differ from those claims approved through the registration process. Therefore, should the Agency find or if it is brought to our attention that a website contains false or misleading statements or claims substantially differing from the EPA approved registration, the website will be referred to the EPA's Office of Enforcement and Compliance.

If you fail to satisfy these data requirements, EPA will consider appropriate regulatory action including, among other things, cancellation under FIFRA section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Please note that the record for this product currently contains the following CSFs:

- Basic CSF dated 2/4/2016

If you have any questions, please contact Rita Kumar by phone at (703) 308-8291, or via email at kumar.rita@epa.gov.

Enclosure: Stamped label

EPA REG. NO. 83399-RA
INITIAL PRODUCT REGISTRATION
DATE: Feb. 08, 2016

> ***"Master Label"***
> *This master label includes label text for different size packages and application rates specific to the pet's age and body weight. Text that appears in parenthesis are informational to the EPA, but will not be printed. Text that appears in brackets are optional.*

FRONT PANEL

(Market Label-

- *The word Cat will be at least 40-75% in height of the largest letter in the primary brand name.*
- *A large clear picture of a cat in the respective weight range will be on the front panel of the label.)*

Imidacloprid and Pyriproxyfen Spot-On Solution for Cats

Alternate Brand Names include:
Combiva II For Cats
Combiva II For Cats and Kittens
CrossBlock II For Cats
CrossBlock II For Cats and Kittens
CAH17 for Cats and Kittens
(The above brand names will be packaged in the weight ranges below:)
2-5 lbs., 8 weeks or older (0.0078 fl oz)
5- 9 lbs., 8 weeks or older (0.014 fl oz)
Over 9 lbs. (0.027 fl oz)

ACCEPTED
Feb 08, 2016
Under the Federal Insecticide, Fungicide and Rodenticide Act as amended, for the pesticide registered under EPA Reg. No. 83399-16

Imidacloprid and Pyriproxyfen Spot-On Solution for Cats Treats and Prevents Further Flea Infestation on Cats and kittens 8 weeks and older

ACTIVE INGREDIENTS:	
Imidacloprid	9.10%
Pyriproxyfen	0.46%
OTHER INGREDIENTS:	90.44%
TOTAL	100.00%

NET CONTENTS: **XXX fl oz (XXX mL)**
[XX Doses [each dose XXX fl oz]]

EPA Est. No. TBD **EPA Reg. No. 83399—NEW**

KEEP OUT OF REACH OF CHILDREN
CAUTION

SeeBack Panel / Package Insert for additional Precautionary Statements, First Aid and Directions for Use.

Use only on cats [and] [kittens] weighing (insert product weight range) lbs. and 8 weeks of age or older

Information in [ ] is optional

BACK PANEL & INSERT LANGUAGE

READ ENTIRE LABEL BEFORE EACH USE
USE ONLY ON CATS AND KITTENS 8 WEEKS OR OLDER WEIGHING AT LEAST 2 LBS

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Keep out of reach of children.

HAZARDS TO DOMESTIC ANIMALS.

FOR EXTERNAL USE ON CATS ONLY. DO NOT USE ON DOGS.

Do not use on kittens under 8 weeks of age or weighing less than 2 lbs. Do not treat your cat with more than one pesticide product at a time. As with any product, consult a veterinarian before using this product on debilitated, aged, medicated, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any pesticide product.

FIRST AID	
IF SWALLOWED:	Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything to an unconscious person.
IF IN EYES:	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
IF ON SKIN OR CLOTHING:	Wash with plenty of soap and water. Remove and wash contaminated clothing before reuse
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may contact 1-800-999-0297 weekdays between 9am and 6pm EST or 1-888-426- 4435 for emergency medical treatment information.	

Side Effects: Monitor your cat after application. Although side effects are rare, some cats may experience some temporary irritation at the site of the product application such as redness, scratching or other signs of discomfort. If these or other side effects occur, consult your veterinarian or call 1-800-999-0297. If your cat has an unusual reaction to the initial application, consult a veterinarian before repeating application. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have been reported.

Information in [ ] is optional

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

CONSUMER INFORMATION

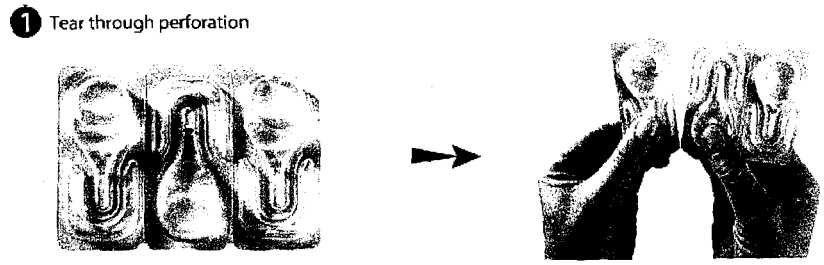
[Imidacloprid and Pyriproxyfen Spot-On Solution for Cats [This product] kills fleas within 12 hours, and re-infesting fleas are killed within 2 hours. **Imidacloprid and Pyriproxyfen Spot-On Solution for Cats** prevents further flea infestation for four [4]weeks [1 month][30 days]. [The active ingredients in] Imidacloprid and Pyriproxyfen Spot-On Solution for Cats [this product] are formulated for control of fleas for 1 month[4 weeks][30 days] on cats. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is an effective flea adulticide, larvicide, and ovicide [that [kills] [prevents][,treats] [,and][controls] fleas.]

RESTRICTIONS:

- Do not allow children to apply product.
- For use only on cats [and kittens] 8 weeks and older.
- Do not use on other animals.
- Do not apply to cats [or kittens] weighing less than 2 lbs (0.0078 fl. oz.) [5 lbs. (0.014 fl. oz.)] [9 lbs. (0.027 fl. oz.)]
- Weigh your cat to be sure you are using the right size product for your cat.
- Do not apply more than one [1] tube per treatment, even for larger cats.
- Do not split one tube between two cats.
- Do not have contact or allow children to have contact with treated area until completely dry.

TO PREVENT HARM TO YOU AND YOUR CAT, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. FOR EXTERNAL USE ON CATS ONLY. DO NOT USE ON OTHER ANIMALS.

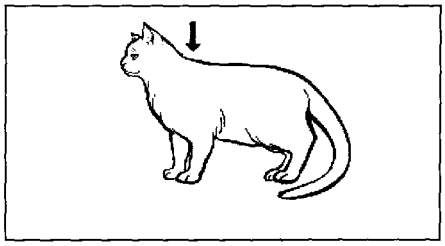
OPENING INSTRUCTIONS:



Information in [ ] is optional

HOW TO APPLY:

1. The cat should be standing or in a comfortable position for easy application.
2. Part the hair down to the level of the skin, and slowly apply the product at the base of the cat's head until the applicator is completely empty. (Avoid superficial application to the cat's hair).



3. Do not get the product in the cat's eyes or mouth. Do not allow your cat to ingest this product. Salivation may occur if the cat ingests the product immediately after treatment. Do not use more than one tube on cats greater than 9 lbs.
4. Discard the empty applicator as outlined in the Storage and Disposal section.
5. Repeat every month, or as recommended by your veterinarian.

FREQUENCY OF APPLICATION

The presence of fleas on cats may cause a sensitive skin disorder due to the feeding activity of fleas. This is called flea allergy dermatitis [FAD]. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats kills fleas that may cause flea allergy dermatitis [FAD]. Treatment of Imidacloprid and Pyriproxyfen Spot-On Solution for Cats will kill fleas on cats [and][kittens] within twelve [12] hours. It is possible pre-existing pupae in the environment may continue to emerge for six [6] weeks [or longer] depending on climatic conditions. Use Imidacloprid and Pyriproxyfen Spot-On Solution for Cats monthly [every 30 days][every 4 weeks] for the control of fleas.

OR

[Studies have shown that] Imidacloprid and Pyriproxyfen Spot-On Solution for Cats kills fleas on cats within 12 hours for up to four [4] weeks [1 month][30 days]]. To prevent flea re-infestation, apply monthly. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats remains effective even after exposure to sunlight. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is water resistant and is still effective, after bathing or water immersion. Allow treated area to dry thoroughly.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: Store in a cool, dry place. Keep out of reach of children.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: Non-refillable container. Do not reuse or refill this container. **If empty:** Place in trash or offer for recycling, if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

Information in [ ] is optional

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Seller warrants that the material conforms to the chemical parameters of the US EPA registration and the label. To the extent consistent with applicable law, seller makes no warranty, express or implied, other than indicated on the label. Buyer and user assume all risk of use and handling of this material. To the extent consistent with applicable law, any damages arising from use of this product or a breach of this warranty shall be limited to direct damages and shall not include consequential or incidental damages such as loss of profit or values.

[Made in Germany]

[Distributed by:] [Manufactured by:]
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

EPA Reg. No. **83399**-NEW
EPA Est. No. **TBD**
[lot#, date &/or label code] [UPC CODE]

Optional Marketing Claims

(for use on the front, side, or back panels of the outer box or on the package insert)

- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] contains the active ingredient imidacloprid,[and an/the] [insect growth regulator][IGR] pyriproxyfen
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] contains [insect growth regulator] [IGR] that effectively kills flea eggs
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] prevents further flea infestation for four[4] weeks [1 month][30 days]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] prevents further flea infestation for up to four [4] weeks [1 month][30 days]
- Protects against fleas
- Protects against further flea infestation up to four[4] weeks [1 month][30 days]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats helps prevent further flea infestation for up to four [4] weeks [1 month][30 days]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats [continually] works to prevent further flea infestation for up to four [4] weeks [1 month][30 days]
- [Effectively] [stops][controls] existing flea infestation by killing adult fleas][and prevents further re-infestation]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] treats, controls, and prevents flea re-infestation
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] treats fleas [within 12 hours] on cats and kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Kills fleas within [in] 12 [twelve] hours [after application]
- Kills fleas before egg laying
- Kills fleas before eggs can be laid
- Kills fleas on cats and kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Kills fleas and their eggs
- Effectively kills flea eggs
- Disrupts the flea cycle and kills larval flea stage

Information in [ ] is optional

- Breaks the flea life cycle [and][prevents][stops] flea eggs from developing into adult [biting] fleas
- Kills flea eggs from hatching[and][developing into biting adults]
- Larval flea stages are killed after Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is applied to cats or kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Kills flea larvae on cats and kittens 8 weeks or older weighing at least 2 pounds [lbs] after contact [treatment] with Imidacloprid and Pyriproxyfen Spot-On Solution for Cats
- Kills re-infesting fleas within 2 hours [and][Protects against further flea infestations [up to four [4] weeks][one month][30 days]]
- Prevents further re-infestations by killing adult fleas within 12 hours for up to one month [4 weeks] [30 days]
- Controls fleas for cats and kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Treats flea infestation on cats and kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Provides flea protection [up to [[four][4] weeks][a month][30 days]]
- Controls against problematic fleas
- Kills fleas that may cause flea allergy dermatitis (FAD)
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] offers 3-way flea protection that [kills][[controls][prevents] against] adults, larvae, and eggs
- [An effective] flea adulticide, larvicide, and ovicide [that [kills][prevents][,treats][,and][controls] against fleas]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] offers effective multistage flea control
- Effective once a month flea [protection][prevention and treatment]
- Effective flea treatment for your cat 8 weeks of age or older weighing at least 2 pounds [lbs]
- Monthly topical treatment of Imidacloprid and Pyriproxyfen Spot-On Solution for Cats kills fleas and treats flea infestation for cats and kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Monthly treatment prevents further reinfestation and treats fleas on cats and kittens 8 weeks or older weighing at least 2 pounds [lbs]
- Formulated to target every stage of flea development [to treat and prevent further flea infestations]

All Others

- For Cats and Kittens 8 weeks or older weighing at least 2 pounds [lbs]
- For use on kittens 8 weeks or older weighing at least 2 pounds [lbs]
- For use on cats only 8 weeks or older weighing at least 2 pounds [lbs]
- Easy to Use Applicator
- Easy to Apply Applicator
- Applies Easily
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats recommends monthly treatments
- One Step Flea Prevention for up to [[four][4] weeks] [a month][30 days]
- For Best Results Apply [Monthly][30 Days][every[4][four] weeks]
- For year round protection apply monthly [every [[four] [4] weeks] [30 days]]
- Use [Monthly][Every[30 Days][4][Four]Weeks] for Best Results
- Only one treatment needed every month [30 days][[4][four] weeks]]
- One treatment remains effective for 4[four] weeks[1 month][30days]
- Water-resistant after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is waterproof after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is effective after [bathing] [shampooing]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is effective [even] after exposure to rain or sunlight
- Formulated for control of fleas for 1 month [4 weeks] on cats
- Contains the [same] active ingredients [imidacloprid, pyriproxyfen] as in [Bayer] Advantage II for Cats

- Contains the active ingredients found in [Bayer] Advantage II for cats
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is not manufactured or distributed by Bayer [Animal Health]

APPLICATOR LABELING

{Front Label}	{Back Label}
Imidacloprid and Pyriproxyfen Spot-On Solution For Cats [insert wt range] lbs 8 weeks or older Imidacloprid 9.10% Pyriproxyfen 0.46% XXX fl. oz. {label code}	KEEP OUT OF REACH OF CHILDREN CAUTION Read entire label before use. [Use scissors to open.] EPA REG. No. 83399-NEW Lot # (*designation will identify producing establishment*) {label code}

Information in [ ] is optional

Kumar, Rita

From: Meadows, Sarah
Sent: Thursday, February 11, 2016 11:21 AM
To: OPP RD QAQC; Eagle, Venus; Kumar, Rita
Subject: QAQC Pass 83399-16
Attachments: 83399-16-20160208.pdf

The above product has passed the quality control check. Please print the e-signed letter/e-stamped label (attached), file the hard copy in the jacket, close the action in OPPIN, and return the jacket to the file room. Include the Data Extraction Request Form for the new CSFs. Please notify me when you have closed the action in OPPIN. Your action can not be uploaded to PPLS until it is closed in OPPIN and the file symbol has been converted to a registration number in the system. Thank you.

Kumar, Rita

From: Kumar, Rita
Sent: Friday, February 05, 2016 12:08 PM
To: 'Katy Hernandez'; Alicia Henk
Cc: Eagle, Venus
Subject: RE: FW: Pre-decisional letters for 83399-RT and 83399-RA

Importance: High

Katy: Please see my comments to revised labels draft dated 2-4-2016:

Dog product (83399-RT), refer to highlighted copy:

1. Page 6, first bullet about flea eggs must be deleted.
2. Page 6, the third bullet is not acceptable as presented. Delete or rephrase to clearly indicate that the product kills adult fleas in within 12 hours and prevents further infestation for four weeks. All the optional permutations are confusing.
3. Page 6, fourth, fifth, and third from last bullets , and elsewhere on the label, age is not optional. Brackets can be for "and puppies", but not the minimum age.
4. On page 6, All Other claims, The bullet about year round use should be rephrased as: "For year round protection, apply monthly" or something similar. Monthly application must be specified in this statement.

Cat product (83399-RA), refer to highlighted copy:

1. Across the board and specially in the marketing claims, wherever flea infestation is mentioned, it must be changed to "further flea infestation".
2. Delete the claim identical to #2 mentioned above. It is a bullet in the middle of page 6.
3. On page 7, third bullet about year round use should be rephrased as: "For year round protection, apply monthly" or something similar. Monthly application must be specified in this statement.
4. On page 7, delete "Specially" from the bullet starting with "Specially formulated for....."

Please submit revised label ASAP.
Thanks,
Rita

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Thursday, February 04, 2016 2:34 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>; Alicia Henk <alicia.henk@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: Re: FW: Pre-decisional letters for 83399-RT and 83399-RA

Rita,
I have attached the updated labels according to the three requests you have sent over the last two days. We will continue working to update the remaining forms. Thank you.

Katy Hernandez

Kumar, Rita

Resubmission
98070 5
83399-RA

From: Katy Hernandez <katy.hernandez@ceva.com>
Sent: Friday, February 05, 2016 1:32 PM
To: Kumar, Rita
Cc: Alicia Henk; Eagle, Venus
Subject: Re: FW: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: Imidacloprid + PPF Dog Label 05Feb2016- clean.pdf; Imidacloprid + PPF Dog Label 05Feb2016- highlighted.pdf; Imidacloprid Cat + PPF Label 04Feb2016- Clean.pdf; Imidacloprid Cat + PPF Label 04Feb2016- Highlighted.pdf

I have attached the updated labels according to your recent comments. Let me know if you need anything further.

Katy Hernandez
Ceva Animal Health, LLC
Regulatory Associate
Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Fri, Feb 5, 2016 at 11:07 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Katy: Please see my comments to revised labels draft dated 2-4-2016:

Dog product (83399-RT), refer to highlighted copy:

1. Page 6, first bullet about flea eggs must be deleted.

2. Page 6, the third bullet is not acceptable as presented. Delete or rephrase to clearly indicate that the product kills adult fleas in within 12 hours and prevents further infestation for four weeks. All the optional permutations are confusing.

3. Page 6, fourth, fifth, and third from last bullets , and elsewhere on the label, age is not optional. Brackets can be for "and puppies", but not the minimum age.

4. On page 6, All Other claims, The bullet about year round use should be rephrased as: "For year round protection, apply monthly" or something similar. Monthly application must be specified in this statement.

Cat product (83399-RA), refer to highlighted copy:

1. Across the board and specially in the marketing claims, wherever flea infestation is mentioned, it must be changed to "further flea infestation".

2. Delete the claim identical to #2 mentioned above. It is a bullet in the middle of page 6.

3. On page 7, third bullet about year round use should be rephrased as: "For year round protection, apply monthly" or something similar. Monthly application must be specified in this statement.

4. On page 7, delete "Specially" from the bullet starting with "Specially formulated for....."

Please submit revised label ASAP.

Thanks,

Rita

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Thursday, February 04, 2016 2:34 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>; Alicia Henk <alicia.henk@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: Re: FW: Pre-decisional letters for 83399-RT and 83399-RA

Rita,

I have attached the updated labels according to the three requests you have sent over the last two days. We will continue working to update the remaining forms. Thank you.

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Form Approved OMB Nos. 2070-0060, 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	83399-RA
Active Ingredient(s) and/or representative test compound(s) Imidacloprid, Pyriproxyfen	Date 02/04/2016
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor non-food	Product Name Imidacloprid & Pyriproxyfen Spot-On Solution for Ca

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☑ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

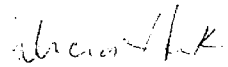
I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (!) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
	02/04/2016	Alicia Henk, Director, Development & Reg. Affairs

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version.

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016	**EPA Reg No./File Symbol:** 83399-NEW	Page 1 of 4
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	

Ingredients: Imidacloprid, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Product Chemistry					
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1750	Group A Product Chemistry for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609001	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution	49609002	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution: Analytical Method Validation Report	49609003		OWN	
830.6302, 830.6303, 830.6304, 830.6313, 830.6314, 830.6315, 830.6316, 830.6319, 830.6321, 830.7000, 830.7100, 830.7300. 830.7520	Summary of Group B Product Chemistry and Waivers for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609004	Ceva Animal Health, LLC	OWN	
830.6302, 830.6303, 830.6304, 830.7100, 830.7300	Physical and Chemical Characteristics: Color, Physical State, Odor, Viscosity, and Density for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609005	Ceva Animal Health, LLC	OWN	
830.6315	Flashpoint for Ceva Animal Health's Imidacloprid Spot-On Solution, Imidacloprid & Pyriproxyfen Spot-On Solution, and Imidacloprid & Permethrin Spot-On Solution	49609006	Ceva Animal Health, LLC	OWN	
Toxicology Data Requirements					
870.1100	Acute Oral Toxicity Study of Imidacloprid Pyriproxyfen Spot On Solution in Sprague-Dawley Rats	49609007	Ceva Animal Health, LLC	OWN	
870.1200	Acute Dermal Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096905	Bayer Animal Health	OLD	
870.1300	Acute Four-Hour Inhalation Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096906	Bayer Animal Health	OLD	
870.2400	Acute Eye Irritation Test of Imidacloprid/Pyriproxyfen Spot On Solution in New Zealand Albino Rabbits	49609008	Ceva Animal Health, LLC	OWN	

Signature	**Name and Title** Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	**Date** **February 4, 2016**

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016	**EPA Reg No./File Symbol:** 83399-NEW	Page 2 of 4
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	

Ingredients: Imidacloprid, Pyriproxyfen

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.2500	Primary Dermal Irritation Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096908	Bayer Animal Health	OLD	
870.2600	Dermal Sensitization Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096909	Bayer Animal Health	OLD	
870.7200	Acute Toxicity Evaluation for Dermal Treatment of Cats with Imidacloprid (Bay t 7391) Spot-On: Lab Project Number: TR-94D-010: 74579. Unpublished study prepared by Miles Inc. Animal Health DeSoto Research Facility. 19 p	43679501	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Bay t 7391) Spot-On On Cats: Lab Project Number: TR-95F-006: 74591. Unpublished study prepared by Bayer Corp. DeSoto Research Facility. 41 p	43679502	Bayer Animal Health	OLD	
870.2600	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Six Week Old Kittens: Lab Project Number: 74746: TR-96F-004: 10332. Unpublished study prepared by Bayer Corp., DeSoto Research Facility. 41 p. Relates to L0000102.	44157301	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Kittens Eight Weeks of Age: Lab Project Number: 74747: TR-96F-006: 10332. Unpublished study prepared by Bayer Corp., DeSoto Research Facility. 45 p. Relates to L0000102.	44157302	Bayer Animal Health	OLD	
870.7200	Acute Oral Toxicity Evaluation of Imidacloprid (Advantage) in Cats: Lab Project Number: TR-96F-011: 74769: J:USERS\LINDA\NOREPORT\JAS0173.RP. Unpublished study prepared by Bayer Corp., Animal Health. 10 p.	44179802	Bayer Animal Health	OLD	
870.7200	Evaluation of the General Safety of M880	47924801	Bayer Animal Health	PAY	
870.7200	Imidacloprid + Pyriproxyfen: Addendum to Bayer Report No. 33714 (MRID 47924801) - Evaluation of the General Safety of M880	48085101	Bayer Animal Health	PAY	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot-on Formulation in the Target Species, Adult Cats	45097001	Bayer Animal Health	OLD	
Product Performance Test Guidelines					
810.3300	Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Cats: Lab Project Number: MIC 194: 74571. Unpublished study prepared by Agresearch Consultants, Inc. 32 p.	43679503	Bayer Animal Health	OLD	

Signature	**Name and Title**	**Date**
	Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	**February 4, 2016**

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016	**EPA Reg No./File Symbol**: 83399-NEW	Page 4 of 4
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	
Ingredients: Imidacloprid, Pyriproxyfen		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Cats: Lab Project Number: PD-7391-95F-004: 74581. Unpublished study prepared by Professional Laboratory and Research Services, Inc. (PLRS). 46 p.	43679504	Bayer Animal Health	OLD	
810.3300	Efficacy Evaluation of BAY t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Adult Fleas and Flea Eggs on Cats: Lab Project Number: BH036/95: 74634: 95REPORT/AUSTRALI.DOC. Unpublished study prepared by Bayer Australia Ltd. 33 p.	43794101	Bayer Animal Health	OLD	
810.3300	Controlled Field Trials on the Efficacy and Tolerance of a Spot-On Formulation of Imidacloprid (BAY NTN 33893) 10% for Control of the Cat Flea (C. felis) in Domestic Cats: Lab Project Number: HVS 95-01: 74635: 95REPORT/74635.DOC. Unpublished study prepared by Institute of Parasitology, Hannover Vet School. 7 p.	43794102	Bayer Animal Health	OLD	
810.3300	Comparative Evaluation of How Quickly Advantage and Frontline (Fipronil) Top Spot Kill Fleas on Dogs: (final Report)	44256901	Bayer Animal Health	OLD	
810.3300	Imidacloprid Topical Formulation: Larvicidal Effect Against Ctenocephalides felis in the Surroundings of Treated Dogs	44256902	Bayer Animal Health	OLD	
810.3300	Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of Advantage for Flea Control on Dogs	44256903	Bayer Animal Health	OLD	
810.3300	Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.	45086801	McLaughlin Gormley King Company	OLD	

Signature	Name and Title	Date
	Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	February 4, 2016

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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WASHINGTON, D.C. 20460

DATA MATRIX

Date: February 4, 2016		**EPA Reg No./File Symbol:** 83399-NEW		Page 4 of 4	
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215		**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats			
Ingredients: Imidacloprid, Pyriproxyfen					
Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Imidacloprid and Pyriproxyfen Generic Data for Companion Animal Use					
875.1200, 875.2100, 875.2400	Evaluation of Potential Exposures to Pet Owners and Veterinary Professionals During Application of ADVANTAGE to Control Fleas on Cats and Dogs: Lab Project Number: 106743. Unpublished study prepared by Bayer Corp. 50 p.	43790701	Bayer Healthcare, LLC	OLD	
	Imidacloprid (Bay t 7391) – Stroke Test in Dogs after Topical Application of Imidacloprid Spot-on 10%; Bayer Animal Health Development AH-D ID: 16051; Unpublished study		Bayer Healthcare, LLC	PAY	
	Evaluation of the Toxicology and Potential Health Risks Associated with Indoor, Nonfood Uses of Sumilarv; J. Driver, S. Oonnithan, O. Paynter, et al. (1991) Unpublished study prepared by Technology Services Group, Inc. 71 p.	42182701	McLaughlin Gormley King Company	OLD	
870.3200	S31183: Toxicity Study by Oral (Capsule) Administration to Beagle Dogs for 52 Weeks (Sumilarv Technical Grade): Lab Project Number: 91/0776. Unpublished study prepared by Life Science Research Ltd. 320 p.	42178309	McLaughlin Gormley King Company	OLD	
Signature	**Name and Title** Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC			**Date** **February 4, 2016**	

Kumar, Rita

Resubmission; S 83399-RA

From: Katy Hernandez <katy.hernandez@ceva.com>
Sent: Thursday, February 04, 2016 2:34 PM
To: Kumar, Rita; Alicia Henk
Cc: Eagle, Venus
Subject: Re: FW: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: Imidacloprid + PPF Dog Label 04Feb2016- Clean.pdf; Imidacloprid + PPF Dog Label 04Feb2016- Highlighted.pdf; Imidacloprid Cat + PPF Label 04Feb2016- Clean.pdf; Imidacloprid Cat + PPF Label 04Feb2016- Highlighted.pdf

Rita,
I have attached the updated labels according to the three requests you have sent over the last two days. We will continue working to update the remaining forms. Thank you.

Katy Hernandez
Ceva Animal Health, LLC
Regulatory Associate
Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Thu, Feb 4, 2016 at 10:26 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Katy: Please see the following for the data comp issues:

1. You sent us a revised data matrix with additional citations for generic data to support companion animal use. Please send us an updated data citation form with the same date as the data matrix.

2. The alternate source for imidacloprid is [redacted] active, whereas the basic source is [redacted] Please explain how you made up the difference in active percentage.

3. The Agency used generic data to make the determination that pyriproxyfen was acceptable for companion animal use. Therefore you must cite or submit generic data for this use. As explained by us to you in a conference call two weeks ago, doing a cite-all for generic data - companion animal use, and making an offer to pay might be the best way for you to address this data gap.

In addition, There is one more label comment for both products: Add these two notes on the front panel of the draft label above product name:

Market label - the word Cat (or Dog) will be at least 40-75% in height of the largest letter in the primary brand name.

Market label - a large clear picture of a cat (or dog) in the respective weight range will be on front panel of the label.

Please submit revised labels, along with revised data matrix and data compensation forms to me ASAP. You must also provide an explanation for #2 above, or delete the alternate source for imidacloprid, and revised your formulator's exemption form accordingly.

Thanks,

Rita

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 4:48 PM
To: 'Katy Hernandez' <katy.hernandez@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: FW: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Hi Katy: Further to below, the following additional changes need to be made on the dog label (83399-RT).

1. Delete the claim: "Kills (and)(controls) fleas at all life stages" and any other claims that refer to all life stages.

2. Delete the claim: "[Specially] Formulated to target[s] every stage of flea development [to treat and prevent flea infestation].

3. Some optional marketing claims on page 6 have [7 weeks or older] as optional. The age reference cannot be optional, please remove brackets.

4. Delete "irritating" and "annoying" from the claim: "Controls [against] [problematic] [irritating] [annoying] flea bites".

The following changes must be made in the Cat label (83399-RA). Please refer to highlighted copy of the draft dated 1/29/2016:

1. On the front panel, page 1, Over 9 lbs. is missing a bracket.

2. On page 2, under Consumer Information, last sentence, delete "against". This is not appropriate with rest of the sentence, does not read right!

3. On page 4, under How to Apply, make the following changes in items numbers given below:

5. Delete the second and third sentences, and replace with the original statement: "Repeat every month, or as recommended by your veterinarian." This is more appropriate, since a veterinarian can determine the severity of infestation and specify the frequency of application.

4. On page 6, Delete the claim: "Prevents [re]infestation by killing adult fleas before [they lay eggs][egg laying][eggs can be laid]".

5. In the Other Claims, last bullet on page 7, change "Compare" to "Contains". Compare is not allowed.

Please submit revised labels for both products. We are still working on the data compensation issue for the source products, and will inform you as soon as a decision has been made.

Regards,

Rita

From: Kumar, Rita
Sent: Wednesday, February 03, 2016 11:35 AM
To: 'Katy Hernandez' <katy.hernandez@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: RE: Pre-decisional letters for 83399-RT and 83399-RA
Importance: High

Dear Katy: The following changes need to made in the proposed draft dated 1/29/2016. Refer to the highlighted copy for page numbers.

1. You must submit a picture of the cat icon with the language, on page one and elsewhere. It can be in black and white on the draft label, On page provided you specify the size and colors that will be used on the final printed copy.

2. On page 4, under How to Apply, make the following changes in items numbers given below:

1. Change the last part of last sentence to read: "from the shoulder to the middle of back." Also change the graphic accordingly. The third dot must be applied no further than middle of back to prevent ingestion by the animal.

5. Delete the second and third sentences, and replace with the original statement: "Repeat every month, or as recommended by your veterinarian." This is more appropriate, since a veterinarian can determine the severity of infestation and specify the frequency of application.

3. In the Optional marketing claims, sixth bullet on page 5, change "prevents flea infestation" to "prevents further flea infestation". This change must be made elsewhere also, wherever this kind of statement appears. This product only prevents further flea infestation.

4. In the Optional marketing claims, sixth bullet on page 6, delete "[against]". This is not appropriate with rest of the sentence, does not read right!

5. In the Other Claims, eleventh bullet on page 7, delete "Specially". This indicates heightened efficacy, and is a false claim, since there are many other products with same formulation in the market.

6. In the Other Claims, last bullet on page 7, change "Compare" to "Contains". Compare is not allowed.

I may have some more comments, and I will let you know as soon as I hear from the scientists.

Regards,

Rita

From: Katy Hernandez [mailto:katy.hernandez@ceva.com]
Sent: Friday, January 29, 2016 6:13 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>
Cc: Alicia Henk <alicia.henk@ceva.com>; Eagle, Venus <Eagle.Venus@epa.gov>
Subject: Re: Pre-decisional letters for 83399-RT and 83399-RA

We have attached our response to the predecisional letter for the dog product in this email. This response includes the attached updated documents and forms. Please let me know if these also need to be sent in through the front office.

Katy Hernandez

Ceva Animal Health, LLC

Regulatory Associate

Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Fri, Jan 22, 2016 at 9:20 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Dear Alicia and Katy: Please see attached pre-decisional letters for these two spot-on products. Best Regards,

Rita

Kumar, Rita

Resubmission: S980580 RT ~~83399-RA~~

From: Katy Hernandez <katy.hernandez@ceva.com>
Sent: Friday, January 29, 2016 6:14 PM
To: Kumar, Rita
Cc: Alicia Henk; Eagle, Venus
Subject: Re: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: Cover Letter for Response 29Jan2016- Cat 83399-RA.pdf; Final Response Document Cat.pdf; Revised 1-28-2016 8570-4 Basic CSF for Imidacloprid + PPF Spot-On Solution for Cats.pdf; 20160125 8570-35 Data Matrix Imid + PPF for Cats_revised.pdf; 20160125 8570-35 Data Matrix Imid + PPF for Cats_PUBLIC_revised.pdf; Revised 1-28-2016 8570-27 Imid + PPF for Cats.pdf; Imidaclprid Cat + PPF Label- Highlighted.pdf; Imidaclprid Cat + PPF Label.pdf

We have attached a response to the predecisional letter for the cat product in this email. This response includes the attached updated documents and forms. Please let me know if these also need to be sent in through the front office.

Katy Hernandez
Ceva Animal Health, LLC
Regulatory Associate
Development & Regulatory Affairs
8735 Rosehill Rd, Suite 300
Lenexa, KS 66215
913-945-4458

On Fri, Jan 22, 2016 at 9:20 AM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

Dear Alicia and Katy: Please see attached pre-decisional letters for these two spot-on products. Best Regards,

Rita

*** Pages 32-48 Claimed confidential by submitter***

EPA REG. NO. 83399-RA
INITIAL PRODUCT REGISTRATION
DATE: Jan. 29, 2016

"Master Label"
(This master label includes label text for different size packages and application rates specific to the pet's age and body weight. Text that appears in parenthesis or brackets is optional.)

FRONT PANEL

Picture of cat/kitten according to weight range

Imidacloprid and Pyriproxyfen Spot-On Solution for Cats

Alternate Brand Names include:
CAH17 for Cats and Kittens
Combiva II for Cats
Combiva II for Cats and Kittens
[The above brand names will be packaged in the weight ranges below:]

2-5 lbs., 8 weeks or older (0.0078 fl oz)
5- 9 lbs., 8 weeks or older (0.014 fl oz)
Over 9 lbs. (0.027 fl oz

Imidacloprid and Pyriproxyfen Spot-On Solution for Cats Treats and Prevents Further Flea Infestation on Cats (and Kittens)

ACTIVE INGREDIENTS:	
Imidacloprid	9.10%
Pyriproxyfen	0.46%
OTHER INGREDIENTS:	90.44%
TOTAL	100.00%

NET CONTENTS: **XXX fl oz (XXX mL)**
[XX Doses [each dose XXX fl oz]]

EPA Est. No. TBD **EPA Reg. No. 83399—NEW**

KEEP OUT OF REACH OF CHILDREN
CAUTION

SeeBack Panel / Package Insert for additional Precautionary Statements, First Aid and Directions for Use.

Use only on cats [and] [kittens] weighing (insert product weight range) lbs. and 8 weeks of age or older

Information in [ ] is optional

BACK PANEL & INSERT LANGUAGE

READ ENTIRE LABEL BEFORE EACH USE
USE ONLY ON CATS

IMPORTANT CONSUMER INFORMATION

[Imidacloprid and Pyriproxyfen Spot-On Solution for Cats [This product] kills fleas within 12 hours, and re-infesting fleas are killed within 2 hours. **Imidacloprid and Pyriproxyfen Spot-On Solution for Cats** prevents flea infestation for four [4]weeks [1 month][30 days]. [The active ingredients in] Imidacloprid and Pyriproxyfen Spot-On Solution for Cats [this product] are formulated for control of fleas for 1 month[4 weeks][30 days] on cats. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is an effective flea adulticide, larvicide, and ovicide [that [kills] [prevents][,treats] [,and][controls] against fleas.]

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS

CAUTION: Harmful if swallowed. Causes moderate eye irritation. Avoid contact with eyes or clothing. Wash hands thoroughly with soap and warm water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Keep out of reach of children.

HAZARDS TO DOMESTIC ANIMALS.

FOR EXTERNAL USE ON CATS ONLY. DO NOT USE ON DOGS.

Do not use on kittens under 8 weeks of age or weighing less than 2 lbs. Do not treat your cat with more than one pesticide product at a time. As with any product, consult a veterinarian before using this product on debilitated, aged, medicated, pregnant or nursing cats. Individual sensitivities, while rare, may occur after using ANY pesticide product for cats. If signs persist, or become more severe, consult a veterinarian immediately. If your cat is on medication, consult your veterinarian before using this or any pesticide product.

FIRST AID	
IF SWALLOWED:	Call a poison control center or doctor immediately for treatment advice. Have a person sip a glass of water if able to swallow. Do not induce vomiting unless told to do so by the poison control center or doctor. Do not give anything to an unconscious person.
IF IN EYES:	Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. Call a poison control center or doctor for treatment advice.
IF ON SKIN OR CLOTHING:	Wash with plenty of soap and water. Remove and wash contaminated clothing before reuse
Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may contact 1-800-999-0297 weekdays between 9am and 6pm EST or 1-888-426- 4435 for emergency medical treatment information.	

Information in [ ] is optional

Side Effects: Monitor your cat after application. Although side effects are rare, some cats may experience some temporary irritation at the site of the product application such as redness, scratching or other signs of discomfort. If these or other side effects occur, consult your veterinarian or call 1-800-999-0297. If your cat has an unusual reaction to the initial application, consult a veterinarian before repeating application. Gastrointestinal signs such as hypersalivation, vomiting or diarrhea have been reported.

DIRECTIONS FOR USE

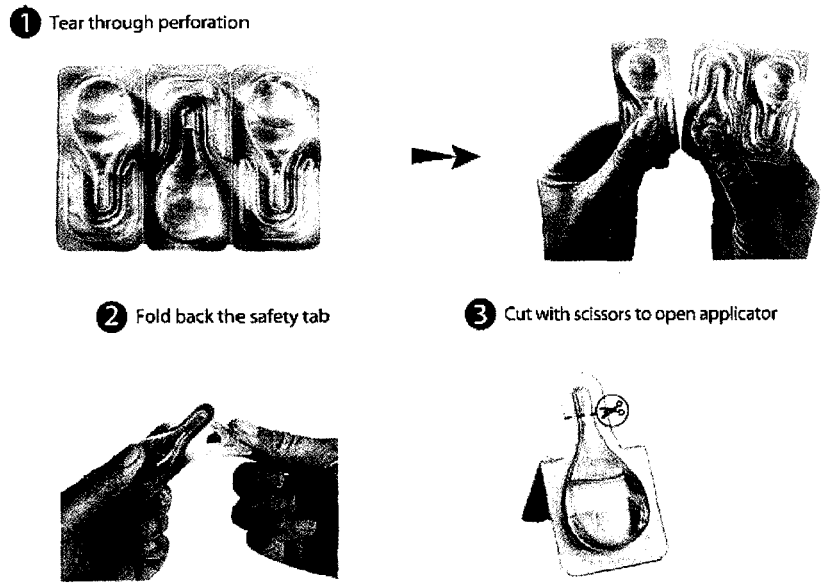
It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

RESTRICTIONS.

- Do not allow children to apply product.
- For use only on cats [and kittens] 8 weeks and older.
- Do not use on other animals.
- Do not apply to cats [or kittens] weighing less than 2 lbs (0.0078 fl. oz.) [5 lbs. (0.014 fl. oz.)] [9 lbs. (0.027 fl. oz.)]
- Weigh your cat to be sure you are using the right size product for your cat.
- Do not apply more than one [1] tube per treatment, even for larger cats.
- Do not split one tube between two cats.
- Do not have contact or allow children to have contact with treated area until completely dry.

TO PREVENT HARM TO YOU AND YOUR CAT, READ ENTIRE LABEL BEFORE EACH USE. FOLLOW ALL DIRECTIONS AND PRECAUTIONARY STATEMENTS CAREFULLY. FOR EXTERNAL USE ON CATS ONLY. DO NOT USE ON OTHER ANIMALS.

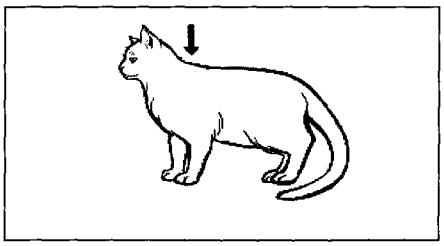
OPENING INSTRUCTIONS:



Information in [ ] is optional

HOW TO APPLY:

1. The cat should be standing or in a comfortable position for easy application.
2. Part the hair down to the level of the skin, and slowly apply the product at the base of the cat's head until the applicator is completely empty. (Avoid superficial application to the cat's hair).



(alternate brand name graphic may vary)

3. Do not get the product in the cat's eyes or mouth. Do not allow your cat to ingest this product. Salivation may occur if the cat ingests the product immediately after treatment. Do not use more than one tube on cats greater than 9 lbs.
4. Discard the empty applicator as outlined in the Storage and Disposal section.
5. Under normal conditions the product is effective for a month. However, in case of severe flea infestation, retreatment may be necessary earlier than four weeks. Do not re-treat more often than once every seven (7) days. After flea control is obtained, return to a monthly retreatment schedule.

FREQUENCY OF APPLICATION

The presence of fleas on cats may cause a sensitive skin disorder due to the feeding activity of fleas. This is called flea allergy dermatitis (FAD). Imidacloprid and Pyriproxyfen Spot-On Solution for Cats kills fleas that may cause flea allergy dermatitis (FAD). Treatment of Imidacloprid and Pyriproxyfen Spot-On Solution for Cats will kill fleas on cats [and][kittens] within twelve [12] hours. It is possible pre-existing pupae in the environment may continue to emerge for six [6] weeks [or longer] depending on climatic conditions. Use Imidacloprid and Pyriproxyfen Spot-On Solution for Cats monthly [every 30 days][every 4 weeks] for the control of fleas.

OR

[Studies have shown that] Imidacloprid and Pyriproxyfen Spot-On Solution for Cats kills fleas on cats within 12 hours for up to four [4] weeks [1 month][30 days]]. To prevent flea [re]infestation, apply monthly. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats remains effective even after exposure to sunlight. Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is water resistant and is still effective, after bathing or water immersion. Allow treated area to dry thoroughly.

STORAGE AND DISPOSAL

Do not contaminate water, food or feed by storage or disposal.

PESTICIDE STORAGE: Store in a cool, dry place. Keep out of reach of children.

PESTICIDE DISPOSAL AND CONTAINER HANDLING: Non-refillable container. Do not reuse or refill this container. **If empty:** Place in trash or offer for recycling, if available. **If partly filled:** Call your local solid waste agency for disposal instructions. Never place unused product down any indoor or outdoor drain.

LIMITED WARRANTY AND LIMITATION OF DAMAGES

Seller warrants that the material conforms to the chemical parameters of the US EPA registration and the label. To the extent consistent with applicable law, seller makes no warranty, express or implied, other than indicated on the label. Buyer and user assume all risk of use and handling of this material. To the extent consistent with applicable law, any damages arising from use of this product or a breach of this warranty shall be limited to direct damages and shall not include consequential or incidental damages such as loss of profit or values.

[Made in Germany]

[Distributed by:] [Manufactured by:]
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

EPA Reg. No. **83399**-NEW
EPA Est. No. **TBD**
[lot#, date &/or label code] [UPC CODE]

Optional Marketing Claims

(for use on the front, side, or back panels of the outer box or on the package insert)

- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] contains the active ingredient imidacloprid,[and an/the] [insect growth regulator][IGR] pyriproxyfen
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] contains [insect growth regulator] [IGR] that effectively kills flea eggs
- **[Imidacloprid and Pyriproxyfen Spot-On Solution for Cats]** prevents flea infestation for four[4] weeks [1 month][30 days]
- **[Imidacloprid and Pyriproxyfen Spot-On Solution for Cats]** prevents flea infestation for up to four [4] weeks [1 month][30 days]
- Protects against fleas
- Protects against flea infestation up to four[4] weeks [1 month][30 days]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats helps prevent further flea infestation for up to four [4] weeks [1 month][30 days]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats [continually] works to prevent flea infestation for up to four[4] weeks [1 month][30 days]
- [Effectively] [stops][controls] existing flea infestation by killing adult fleas][and prevents further reinfestation]

Information in [ ] is optional

- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] treats, controls, and prevents flea reinfestation
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] treats fleas [within 12 hours] on cats and kittens [8 weeks or older]
- Kills fleas within [in] 12 [twelve] hours [after application]
- Kills fleas before egg laying
- Kills fleas before eggs can be laid
- Kills fleas on cats and kittens
- Kills fleas and their eggs
- Effectively kills flea eggs
- Disrupts the flea cycle and kills larval flea stage
- Breaks the flea life cycle [and][prevents][stops] flea eggs from developing into adult [biting] fleas
- Kills flea eggs from hatching[and][developing into biting adults]
- [Kills][and][controls] fleas at all life stages
- Larval flea stages are killed after Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is applied to cat
- Kills flea larval stage after contact [treatment] with Imidacloprid and Pyriproxyfen Spot-On Solution for Cats
- Larval flea stages are killed after contact with [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] treated cat
- Prevents [re]infestation by killing adult fleas before [they lay eggs][egg laying][eggs can be laid]
- Kills re-infesting fleas within 2 hours[and][Protects against further flea infestation [up to four [4] weeks][one month][30 days]]
- Prevents [recurring] [re]infestation[s] by killing adult fleas [within 12 hours][and continues to prevent [re]infestation for up to four [4] weeks [one month][30 days]]
- Controls fleas for cats and kittens [8 weeks or older]
- Treats flea infestation on [cats] [kittens] 8 weeks or older
- Provides flea protection [up to [[four][4] weeks][a month][30 days]]
- Controls against problematic fleas
- Kills fleas that may cause flea allergy dermatitis (FAD)
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] offers 3-way flea protection that [kills][[controls][prevents] against] adults, larvae, and eggs
- [An effective] flea adulticide, larvicide, and ovicide [that [kills][prevents][,treats][,and][controls] against fleas]
- [Imidacloprid and Pyriproxyfen Spot-On Solution for Cats] offers effective multistage flea control
- Effective once a month flea [protection][prevention and treatment]
- Effective flea treatment [for your cat]
- Monthly topical treatment of Imidacloprid and Pyriproxyfen Spot-On Solution for Cats kills fleas and treats flea infestation [for cats 8 weeks or older]
- Monthly treatment prevents further reinfestation and treats fleas on cats 8 weeks or older
- [[Specially] Formulated to] target[s] every stage of flea development [to treat and prevent flea infestation]

All Others

- For Cats and Kittens 8 weeks or older
- For Use on kittens 8 weeks or older
- For Use on Cats Only
- Easy to Use [Applicator]

- Easy to Apply [Applicator]
- Applies Easily
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats recommends monthly treatments
- Easy One Step Flea Prevention for up to [[four][4] weeks] [a month][30 days]
- For Best Results Apply [Monthly][30 Days][every[4][four] weeks]
- Best used year round][once [a month][every [four][4] weeks][30 days]]
- Use [Monthly][Every[30 Days][4][Four]Weeks] for Best Results
- Only One Treatment Needed [Every [Month][30 Days][[4][Four]Weeks]]
- One treatment remains effective for [[4][four] weeks][1 month][30days]
- Water-resistant after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is waterproof after application
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is effective after [bathing] [shampooing]
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is effective [even] after exposure to rain or sunlight
- Specially formulated for control of fleas for 1 month [4 weeks] on cats
- Contains the [exact] [same] active ingredients [imidacloprid, pyriproxyfen] in [Bayer] Advantage II for Cats
- Compare the active ingredients in [Bayer] Advantage II for cats
- Imidacloprid and Pyriproxyfen Spot-On Solution for Cats is not manufactured or distributed by Bayer [Animal Health]

APPLICATOR LABELING

{Front Label}	{Back Label}
Imidacloprid and Pyriproxyfen Spot-On Solution For Cats [insert wt range] lbs 8 weeks or older Imidacloprid 9.10% Pyriproxyfen 0.46% XXX fl. oz. {label code}	KEEP OUT OF REACH OF CHILDREN CAUTION Read entire label before use. (Use scissors to open.) EPA REG. No. 83399-NEW Lot # (*designation will identify producing establishment*) {label code}

Information in [ ] is optional

Kumar, Rita

From: Kumar, Rita
Sent: Friday, January 22, 2016 10:20 AM
To: Alicia Henk; Katy Hernandez
Cc: Eagle, Venus
Subject: Pre-decisional letters for 83399-RT and 83399-RA
Attachments: 83399-RT pre-decisional letter signed 1-22-2016.pdf; 83399-RT label comments rk 1-22-2016.docx; 83399-RA predecisional letter signed 1-22-2016.pdf; 83399-RA label comments rk 1-22-2016.docx

Dear Alicia and Katy: Please see attached pre-decisional letters for these two spot-on products. Best Regards, Rita

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

JAN 2 2 2016

Alicia Henk
Sergeant's Pet Care Products, Inc.
Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

Subject: PRIA Predecisional letter – New product registration
Product Name: Imidacloprid & Pyriproxifen Spot-On Solution for Cats
EPA File Symbol: 83399-RA
Decision Number: 503583

Dear Ms. Henk:

The Agency has completed its review and assessment of your application pursuant to Section 33(b)(3) of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) as amended by the Pesticide Registration Improvement Extension Act of 2012. The Agency has made a pre-decisional determination that your application cannot be approved unless revisions are made to the draft label dated May 14, 2015. The necessary label changes are specified on the attached document.

Since there is limited time before the PRIA Decision Due Date expires, it is important to discuss any objections you have to these changes immediately and whether you will need to submit additional data for review. If these discussions determine that submitting data will be necessary, the PRIA decision due date may need to be renegotiated to allow sufficient time to address and resolve such differences. If the PRIA Decision Due Date is not renegotiated, and the label issues are not resolved before the PRIA Decision Due Date, the Agency will send a follow-up letter that will represent the Agency's decision to close out the PRIA decision review time. The follow-up letter will provide the following three options for continuing the review of the application:

a. You agree to all of the terms associated with the draft accepted label as revised by the Agency and requests that it be issued as the accepted final Agency-stamped label; or
b. You do not agree to one or more of the terms of the draft accepted label as revised by the Agency and requests additional time to resolve the difference(s); or
c. You withdraw the application without prejudice for subsequent resubmission, but forfeits the associated registration service fee.

If you inform EPA that you have concerns as described under (b) above, you will have up to 30 calendar days from the date of that follow-up letter to reach agreement with the Agency on the final version of the

label that the Agency will accept. If an agreement cannot be reached within those 30 days, EPA would intend to proceed with denial of the application.

If you agree to all of the terms of the accepted label as described in (a) above, or if you and EPA resolve any differences as described in (b), you must submit a revised label to EPA. EPA will then provide an accepted final Agency stamped label to you within 2 business days following your written electronic confirmation of agreement to the Agency including the revised label to be stamped.

If you have any questions, please contact Rita Kumar at kumar.rita@epa.gov or (703) 308-8291.

Sincerely,

Venus Eagle, Product Manager 01
Invertebrate and Vertebrate Branch 3
Registration Division (7505P)
Office of Pesticide Programs

Attachment (1)

Attachment for Predecisional letter for 83399-RA

Label Comments for 83399-RT (Imidacloprid & Pyriproxifen Spot-On Solution for Cats)

1. As indicated to you by e-mail on 1/15/2016, the basic Confidential Statement of Formula (CSF) dated 9/1/2016 is not acceptable, because the source products for imidacloprid and pyriproxyfen are not registered for use on companion animals. You must submit a revised data matrix and data citation form after adding cite-all for generic data for companion animal safety, along with a cite-all offer to pay on the data citation form. Alternatively, you can use a source product for each active that is registered for use on companion animals, provided no other changes are made in composition of the basic CSF. A revised Formulator's Exemption statement is needed if you choose this second option.

2. On page 1, change the referral statement as follows: "see Back Panel/Package Insert for additional precautionary statements, First Aid and Directions for Use".

3. The product name must indicate only the basic name that appears on the application form, and will be use in the Notice of Registration, and it is: Imidacloprid and Pyriproxifen Spot-On Solution for Cats. The alternate brand name can be listed separately under the heading Alternate Brand Name.

4. On page 1, the weight and package size statements must be revised to indicate what package size will be used on what weight animal, remove brackets from these statements. Since you have several package sizes under one registration, the animal's weight must relate to intended package size and minimum age of the animal must be mentioned for each, none of this can be optional.

5. On page 1, change both intended use statements to read as follows: Imidacloprid and Pyriproxifen Spot-On Solution for Cats Treats and Prevents Further Flea Infestation on Cats and....., and remove brackets from the first one. This must not be optional.

6. Across the board, replace [Name of Product] with basic product name.

7. On page 2, under First Aid, reverse the order of If Swallowed and If In Eyes, to be consistent with toxicity categories assigned to the product.

8. Wherever you are referring to multiple product name, the first option, preferably the primary name must not be withinin brackets indicating optional. Similarly, no part of the statement "within 12 hours" can be optional, this statement must appear in its entirety to define the time it takes for product to be effective. Similarly, where multiple choices for control time (four weeks, one month etc.) are given, the first one must not be within brackets.

9. We would like to see the graphic for application to animal.

10. Delete the following claims related to efficacy of the product. These claims are not supported by cited efficacy data:
    - kills infesting fleas within 2 hours, the 2 hrs apply to reinfestation only. (You have made "re" as optional in a few places, that is not acceptable, and the optional brackets be changed)
    - prevents flea infestation for at least 4 weeks [1 month][30 days], (delete "at least")
    - long lasting control
    - effectively stops [ends] existing flea infestation, ("ends" is not acceptable)
    - kills reinfesting fleas before they can lay eggs
    - treatment with product can reduce incidence of flea allergic dermatitis (FAD) or flea bite hypersensitivity (this must be superseded with kills fleas that may cause...(FAD)
    - regular monthly use kills fleas and aids in preventing [FAD][flea bite hypersensitivity][from developing]
    - Kills fleas in less than 24 hours, (because it could be interpreted as a time frame less than 12 hours)
    - Treats, controls and prevents flea infestation (change infestation to reinfestation)
    - Treats [controls] and helps prevent further infestation (change infestation to reinfestation)
    - [Effectively] disrupts the flea life cycle and kills flea larval stages (delete effectively)
    - complete [comprehensive] and effective multistage flea protection (complete and comprehensive are heightened efficacy claims, and must be deleted)
    - monthly treatment prevents and treats fleas on cat 7 weeks or older (change this to prevents further reinfestation and treats....)
    - Studies have shown that product kills fleas on cats within 12 hours for up to 1 month [4 weeks][30 days] before adults start laying eggs (eggs could have been laid prior to application)

11. The following optional marketing claims are acceptable:
    - kills within 12 hours
    - kills reinfesting fleas within 2 hours (note: infesting is not acceptable with the 2 hour timeframe, must always state reinfesting)
    - prevents flea infestation for 4 weeks [1 month][30 days] (the first time description cannot be optional, make this change across the board)
    - [brand name] is an effective flea adulticide, larvicide, and ovicide that kills [prevents][treats][and][controls] against fleas
    - Product is effective after exposure to sunlight, is water resistant, waterproof, and is still effective after bathing, or water immersion.
    - To prevent [re]infestation, apply monthly
    - Contains the active ingredient imidacloprid and the insect growth regulator, pyriproxyfen
    - Contains the IGR that effectively kills eggs

- Protects against fleas [for up to 4 weeks][1 month][30 days]
- Kills fleas in less than 24 hours
- Kills fleas before egg laying
- Kills fleas on cats and puppies
- Kills fleas and their eggs
- Effectively kills eggs
- Disrupts [breaks] the flea life cycle
- Prevents fleas from developing into biting adults
- Kills [controls] flea life [cycles] [stages]
- Prevents eggs from hatching and developing into biting adults
- Kills larval stages of fleas
- Helps prevent recurring [re] infestations by killing adult fleas [within 12 hours], and continues to prevent [re]infestation for 1 month [4 weeks][30 days] (the 1 month time frame is mandatory here)
- Controls fleas for cats and kittens
- [Treats] [controls] [prevents] flea infestation
- Provides flea protection [for 1 month][4 weeks][30 days]
- Controls against problematic fleas
- offers 3 way flea protection [kills][controls][prevents] adults, larvae, and eggs
- offers effective multistage control
- formulated to target stages of flea development to treat and prevent flea development
- [kills] [treats][against] fleas which may serve as an intermediate host for tapeworm

The only reference to FAD should be written in the following manner: this product kills fleas that may cause FAD.

12. For the largest size package, there is no upper weight limit, so add this statement to directions for application: "Do not use more than one tube on cats greater than 55 lbs".

13. Add the following to Restrictions:
    - Do not allow children to apply this product
    - Do not allow your cat to ingest this product
    - Do not reapply for four weeks
    - Revise the statement "Do not apply to cats or kittens weighing less than 2 lbs." by adding weight ranges for different size tubes
    - Use entire contents of the tube on each cat. Do not split one tube between two cats. Do not use multiple tubes on one cat
    - Weigh your cat to be sure you are using the right size tube for your cat
    - Separate your cat from all other cats and cats for 24 hours after treatment

14. All Restrictions must be indicated as bulleted statements for more prominence

15. Delete the following "Fleas" marketing claims:
    - Complete and effective flea protection
    - Comprehensive and effective flea treatment
    - Contain the same active ingredients in Bayer...., or Compare to Bayer..... Comparative claims are not acceptable.

9. Per the implementation of label changes to pet spot on products in 2011:

a. The Front Panel is to have a large clear picture of a cat in the weight range for the product as packaged;

b. The Back Panel: Place the box labeled "Side Effects" at the lower right hand corner of the back panel.

Kumar, Rita

From: Kumar, Rita
Sent: Friday, January 15, 2016 4:23 PM
To: 'Alicia'; Katy Hernandez
Cc: Eagle, Venus
Subject: RE: New dog and cat spot on applications 83399-RT and 83399-RA

Importance: High

Hi Alicia: Hope you are doing well. There is an issue with these two registrations that need your immediate attention. None of the two source products (for imidacloprid and pyriproxifen) are registered for indoor no-food use on companion aniumals. Therefore, please submit a revised data matrix with cite all generic data citation for companion animals with an offer to pay form. This is to cover any generic data that were submitted for use of these two chemicals on companion animals. Please send us the revised data matrix and data citation form ASAP. We will be sending you label comments next week.
Beast Regards,
Rita

From: Alicia [mailto:alicia.henk@ceva.com]
Sent: Monday, May 11, 2015 4:19 PM
To: Kumar, Rita <Kumar.Rita@epa.gov>; Katy Hernandez <katy.hernandez@ceva.com>
Cc: Eagle, Venus <Eagle.Venus@epa.gov>
Subject: Re: New dog and cat spot on applications 83399-RT and 83399-RA

Hi Rita
I am happy to see winter behind us! Bring on the sunshine!
Thanks for your info. I will review the agency comments tonight and revert asap.

Best regards
Alicia

On May 11, 2015, at 2:57 PM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:

> Dear Alicia: I have not communicated with you in a while. Hope you are doing well and enjoying the spring weather.
>
> I am doing a preliminary screen of these two spot-on applications, and have the following comments on the proposed labels:
>
> 1. Delete "[insert product name]", and add proposed product name on the front panel. This label must refer to the primary brand name.
>
> 2. Most of the brackets on the front panel statements and in optional marketing text are unnecessary or redundant, and make the label very confusing. Please simplify this label.
>
> 3. First Aid and Precautionary Statements are mandatory for both label and package insert. Delete the bracketed text from the two bulleted statements.

4. Delete the Optional text statement right below the two bulleted statements.

5. Delete the 3 optional text statements starting with: :Apply to cats.....". Only the sentence above with both minimum age and min weight are correct.

6. Delete brackets from the heading "[optional Marketing Text]".

7. The marketing text should be moved to end of the label. It should appear after the Precautionary statements and directions for use.

8. Delete "Fast Acting", or define it based on supporting efficacy data.

9. Under Directions for Use, the description of container (tube, via, applicator etc.) must match the picture. We suggest you use the term applicator, and delete other terms.

10. The statement regarding volume and pet weight needs to be clarified to reflect different volume and weight combination.

11. On the application form in column 6, indicate the product which was the basis of your proposed labeling and marketing text.

Please submit revised labels for further consideration of these applications. Since these are e-submissions, the revised labels must be uploaded to Documentum, therefore also be submitted on a CD thru front end with a hard copy of the cover letter explaining the changes, Please respond ASAP, so that the correct label can be sent for review. Thanks.

Regards,
Rita

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

MEMORANDUM:

To: Rita Kumar

From: Jacquelyn Marchese, Entomologist Jacquelyn Marchese

Secondary Review: Kevin Sweeney, Senior Entomologist Kevin J. Sweeney

Date: January 11, 2016

Subject: PRODUCT PERFORMANCE DATA EVALUATION RECORD (DER)

~~**THIS DER CONTAINS CONFIDENTIAL BUSINESS INFORMATION, AND SHOULD NOT BE RELEASED TO THE REGISTRANT**~~

Note: MRIDs found to be **unacceptable** to support label claims should be removed from the data matrix.

DP barcode: 428223
Decision no.: 503583
Submission no: 968646
Action code: R315
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution for Cats
EPA Reg. No or File Symbol: 83399-RA
Formulation Type: liquid pet spot-on
Ingredients statement from the label with PC codes included:
Imidacloprid, 9.10% PC: 129032
Pyriproxyfen 0.46% PC: 129099

Application rate(s) of product and each active ingredient (lbs. or gallons/1000 square feet or per acre as appropriate; and g/m^2 or mg/cm^2 or mg/kg body weight as appropriate):

Weight range	Monthly product application rate	Lowest imidacloprid mg/kg*	Lowest pyriproxyfen mg/kg*
2-5 lbs (0.91-2.27 kg)	0.23 mL	10.14	0.512
5-9 lbs (2.27-4.08 kg)	0.4 mL	9.81	0.496
9+ lbs (4.08 kg)	0.8 mL	19.63 and lower	0.992

*density is 1.1 g/mL

Use Patterns: For monthly use on cats to provide protection against fleas. Product should be applied by parting the hair at the base of the head and applying the product to the skin of the cat.

I. Action Requested: Review all 8 cited studies and determine their acceptability in support of the proposed product.

II. Background: This proposed product has been given the R315 PRIA designation and is citing 8 efficacy studies to support this product. The 8 cited studies were recently cited to support 2517-RTL. 2517-RTL contains the same percentage of active ingredients that are proposed for this product, 83399-RA. In the 2517-RTL efficacy review dated 11/12/2015 (DP 427217), MRIDs 43679503, 43679504, 44256901, 44256902 and 44256903 were rated unacceptable, MRID 45086801 was rated partially acceptable, and MRID 43794101 was rated acceptable based on today's scientific standards. However, all of these studies are currently supporting claims against public health pests for products 11556-150, 11556-151, and 11556-152, and therefore, similar claims will be supported until all cat products are called in to be reevaluated for registration review.

III. MRID Summary:

As stated above, MRIDs 43679503, 43679504, 44256901, 44256902 and 44256903 were rated unacceptable, MRID 45086801 was rated partially acceptable, and MRID 43794101 was rated acceptable based on today's scientific standards in a 11/12/2015 review for 2517-RTL (DP 427217), though all are currently supporting claims for 11556-150, 11556-151, 11556-152 and now, 2517-RTL. As 2517-RTL contains the same amount of active ingredient that are proposed for this product, 83399-RA, these studies will not be re-reviewed and will be acceptable here.

IV. LABEL RECOMMENDATIONS:

(1) No changes in the Direction for Use section are suggested

(2) The following marketing claims are acceptable:

- kills within 12 hours
- kills reinfesting fleas within 2 hours (note: *infesting* is not acceptable with the 2 hour timeframe)
- prevents flea infestation for 4 weeks [1 month][30 days]
- [brand name] is an effective flea adulticide, larvicide, and ovicide that kills [prevents] [treats][and][controls] against fleas
- Product is effective after exposure to sunlight, is water resistant, and is still effective after bathing, or water immersion.
- Studies have shown that product kills fleas on cats within 12 hours for up to 1 month [4 weeks][30 days] before adults start laying eggs
- To prevent [re]infestation, apply monthly
- Contains the active ingredient Imidacloprid and the insect growth regulator, pyriproxyfen
- Contains the IGR that effectively kills eggs
- Protects against fleas [for up to 4 weeks][1 month][30 days]
- Treats [controls] and helps prevent further infestation
- Kills fleas in less than 24 hours
- Kills fleas before egg laying
- Kills fleas on cats and kittens
- Kills fleas and their eggs
- Effectively kills eggs
- Disrupts [breaks] the flea life cycle
- Kills [controls] flea life [cycle][stages]
- Prevents fleas from developing into biting adults
- Prevents eggs from hatching and developing into biting adults
- Kills larval stages of fleas
- Helps prevent recurring [re] infestations by killing adult fleas [within 12 hours] and continues to prevent [re]infestation for 1 month [4 weeks][30 days] (the 1 month time frame is mandatory here)
- Controls fleas for cats and kittens
- Provides flea protection [for 1 month][4 weeks][30 days]
- Controls against problematic fleas
- offers 3 way flea protection [kills][controls][prevents] adults, larvae, and eggs
- offers effective multistage control

- complete [comprehensive] and effective multistage flea control (note to PM: this has already been approved, but complete and comprehensive suggest heightened efficacy)
- formulated to target stages of flea development to treat and prevent flea development

Note: on page 4 of 6 on the 5/14/2015 proposed label, there is a paragraph on frequency of application. Most of the paragraph is scientifically accurate, but brackets should be revised to ensure there are no claims that suggest the product is efficacious before 12 hours post application. Also, the only reference to FAD should be written in the following manner: *this product kills fleas that may cause FAD.* (The label must indicate that the product kills the flea, not the corresponding condition).

(3) The following marketing claims are unacceptable:

- kills infesting fleas within 2 hours
- prevents flea infestation for *at least* 4 weeks [1 month][30 days]
- long lasting control
- effectively stops [ends] existing flea infestation
- treatment with product can reduce incidence of flea allergic dermatitis (FAD) or flea bite hypersensitivity (this must be superseded with *kills fleas that may cause*)
- regular monthly use kills fleas and aids in preventing [FAD][flea bite hypersensitivity][from developing]

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

December 14, 2015

MEMORANDUM:

Subject:	Name of Pesticide Product:	IMIDACLOPRID & PYRIPROXYFEN SPOT-ON SOLUTION FOR CATS
	EPA Reg. No. /File Symbol:	83399-RA
	DP Barcode:	DP 428216
	Decision No.:	503584
	Action Code:	R315
	PC Codes:	129099 (Imidacloprid: 9.1%) 129032 (Pyriproxyfen: 0.46%)
From:	Byron T. Backus, Ph.D., Toxicologist CITAB Registration Division (7505P)	Byron T. Backus Dec. 14, 2015
Through:	John Redden, M.S., Senior Risk Assessor CITAB Registration Division (7505P)	JCR
To:	Rita Kumar/Venus Eagle RM 01 IVB3 Registration Division (7505P)	
Registrant:	CEVA ANIMAL HEALTH, LLC	

FORMULATION FROM LABEL:

Active Ingredient(s):	by wt.
129099 Imidacloprid	9.10%
129032 Pyriproxyfen	0.46%
Other Ingredients:	90.44%
TOTAL	100.00%

ACTION REQUESTED: "Please provide a technical screen and full review of submitted and cited acute toxicity data to support registration of this dog spot-on product. This is an e-submission, and all the information is in Documentum: Cover letter, transmittal document, data matrix, CSF and label. Copies of the cover letter and proposed label dated 5/14/2015 are also attached…"

COMMENTS AND RECOMMENDATIONS:

1. To satisfy the acute toxicity data requirements, the registrant is citing (data matrix dated April 17, 2015) the following MRIDs: 49609007 (an acute oral toxicity study dated April 10, 2015) and 49609008 (a primary eye irritation study in rabbits dated April 10, 2015), both submitted for EPA File Symbols 83399-RA and 83399-RT; 45096905 (an acute dermal toxicity study in rats); 45096906 (an acute inhalation toxicity study in rats); 45096908 (a primary dermal irritation study in rabbits; and 45096909 (a dermal sensitization study in guinea pigs; the last four cited studies were conducted on a formulation containing 9.1% Imidacloprid and 0.9% Pyriproxyfen, and were originally submitted to the Agency as supporting data for the Bayer products now registered under EPA Reg. Nos. 11556-125 through -130). These studies have been previously reviewed (TXR 5001579, dated August 30, 2000).

2. The registrant's cover letter dated April 17, 2015 includes the following:

   "This new end-use product contains two EPA registered active ingredients in the same amounts that have been combined in other EPA registered products – Advantage® II for Dogs, EPA Reg. Nos. 11556-128, -125, -127, and -130. Further, although this new end-use product is very similar to the EPA registered products Advantage II for Dogs, the formulation is somewhat different, as demonstrated by the acute oral toxicity of this new end-use product. The acute toxicity of this new end-use product does not meet any of the toxicity criteria specified in 40 CFR 157.22, and thus does not require Child Resistant Packaging."

3. The acute oral toxicity study in MRID 49609007 has been previously reviewed (TXR 5015718, CITAB memorandum dated September 24, 2015 for 83399-17) and classified as acceptable. Five rats were each dosed with 1.45 mL/kg of a test material having a specific gravity of 1.100; so that they were limit dosed at 1595 mg/kg. The first three rats that were dosed all survived; the fourth (dosed at 48 hours after the first three) died, while the fifth (dosed 48 hours after the fourth) survived. While there is no mention (or guidance) for a limit dose of 1600 (or 1595) mg/kg in either the OECD or OCSPP (OPPTS) Guidelines, the OECD guidance for 2000 mg/kg is: "Dose one animal at the test dose. If the animal dies, conduct the main test to determine the LD50." In this study the first rat that was dosed survived. From the results (1/5 died) there is an 81.25% probability that the test material has an $LD_{50} \geq 1595$ mg/kg, and the probability of an $LD_{50} \geq 1500$ mg/kg is greater than 81.25%. Based on these results it is concluded that 83399-RA is in Toxicity Category III for oral toxicity ($LD_{50} > 1595$ mg/kg) and does not require Child Resistant Packaging. It is noted that in previous testing (MRID 45096904) of a formulation containing 9.1% Imidacloprid and 0.9% Pyriproxyfen gave LD_{50} values of 1283 mg/kg for males (95% confidence limits were 680 to 1678 mg/kg) and 1000 mg/kg for females (95% confidence limits were incalculable).

4. The eye irritation study in MRID 49609008 has also previously been reviewed and classified as acceptable (TXR 5015718, CITAB memorandum dated September 24, 2015 for 83399-17). Since all three eyes were positive for conjunctival irritation at 48 hours (with 1/3 positive at 72 hours) and all eyes had completely cleared by day 7, the test material is in toxicity category III for eye irritation.

5. After a comparison of the CSFs for 83399-RA and 83399-RT it is concluded that they are toxicologically similar, and acute toxicity studies accepted to support the registration of one of these formulations will also support the other.

6. After a comparison of the CSFs for 83399-RA and 11556-125 it is concluded that the two formulations are toxicologically similar, so that the four cited studies (MRIDs 45096905, 45096906, 45096908 and 45096909) that were used to support 11556-125 will also support the registration of 83399-RT. These studies were previously reviewed (TXR 5001579, August 30, 2000) and classified as acceptable.

7. All acute toxicity data requirements to support the registration of 83399-RA have been satisfied.

8. The following is the acute toxicity profile for 83399-RA, based on the results of the cited acute toxicity studies:

Acute oral LD_{50} (rat)	Tox. Category III	Cited	MRID 49609007
Acute dermal LD_{50} (rat)	Tox. Category IV	Cited	MRID 45096905
Acute inhalation LC_{50} (rat)	Tox. Category IV	Cited	MRID 45096906
Primary eye irritation (rabbit)	Tox. Category III	Cited	MRID 49609008
Primary dermal irritation (rabbit)	Tox. Category IV	Cited	MRID 45096908
Dermal sensitization (guinea pig)	Non-sensitizer	Cited	MRID 45096909

9. Based on the acute toxicity profile given above, the following is the precautionary and first aid labeling for 83399-RA, as obtained from the Label Review System:

PRODUCT ID #: **083399-00016**

PRODUCT NAME: **IMIDACLOPRID & PYRIPROXYFEN SPOT-ON SOLUTION FOR CATS**

PRECAUTIONARY STATEMENTS

SIGNAL WORD: CAUTION

Hazards to Humans and Domestic Animals:

Harmful if swallowed. Causes moderate eye irritation. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco or using the toilet. Avoid contact with eyes or clothing.

First Aid:

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

FEE

~~DOCUMENT CONTAINS CONFIDENTIAL BUSINESS INFORMATION~~

DP BARCODE No.: 428214; **FILE SYMBOL No.**: 83399-RA; **PRODUCT NAME**: Imidacloprid & Pyriproxyfen Spot-On Solution for Cats; **DECISION No.**:503583; **PC Code(s)**: 129099, 129032; **ACTION CODE**: R315; **FOOD Use**: No

DATE OUT: October 13, 2015

SUBJECT: End Use Product Chemistry Review
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution for cats

FROM: Shyam Mathur, Ph.D
Product Chemistry Team Leader
CITAB/RD (7505P)

10-13-15

TO: Rita Kumar / Venus Eagle, RM 01
I-V Branch-3 / RD (7505P)

Company Name: CEVA Animal Health, LLC
Formulation Type: Insecticide

INTRODUCTION:

The registrant has submitted an application for the registration of the new end use product "Imidacloprid & Pyriproxyfen Spot-On Solutions for Cats". The registrant has submitted a CSF for basic formulation (dated 04-15-2015) and the supporting 830 series group A & group B product chemistry data with MRID Nos. 49609001 & 49609006 and the product label. On the advised of the Agency, the registrant has submitted a revised CSF for basic formulation dated (09-01-2015). CITAB has been asked to determine the acceptability of revised basic CSF and the supporting product chemistry data.

SUMMARY OF FINDINGS:

1. Name of Active Ingredient(s): Imidacloprid (9.1%) and Pyriproxyfen (0.46%)

2. Has the registrant claimed substantial similarity to a registered product?

[ ] Yes; [X] No; [ ] NA; if yes, give the registration number of the cited product.

3. All of the source materials of the active ingredient are derived from registered sources: [X] Yes [ ] No

4. All inert ingredients have been screened by IIAB and found to be approved for the proposed labeled Uses: [X] Yes; [ ] No

5. Confidential Statement of Formula(s):

   [X] Proposed Basic - Dated: 04-15-2015; Re-submitted - Dated: 09-01-2015

   [ ] Proposed Alternate – Dated:; Re-submitted – Dated:

   Alternate CSF(s) complies with 40CFR§152.43: [ ] Yes; [ ] No; [X] NA

6. Product label

   a. Ingredient statement: Nominal concentration of AI listed on CSF(s) concurs with product label

      (PR Notice 91-2)

      [X] Yes, if not, explain below:

      Metallic equivalent: [ ] Yes [X] NA;
      Soluble arsenic: [ ] Yes [X] NA
      Isomeric ratios: [ ] Yes [X] NA;
      Acid equivalent: [ ] Yes [X] NA; acid equivalent =

   b. Health related sub statements: Product contains?

      Petroleum distillate at > 10%: [ ] Yes [X] No [ ] NA
      Methanol at > 4%: [ ] Yes [X] No [ ] NA
      Sodium nitrite/sodium nitrate [ ] Yes [X] No [ ] NA

   c. Physical chemical hazard statement: Product label requires a statement per 40 CFR §156.78 for: flammability, explosive potential or electric insulator breakdown?
      [ ] Yes [x] No

      Is the sub statement in compliance with PR Notice 97-6? [ ] Yes, [x] NA; [ ] No; if not, explain Below:

      d. Label requires an additional Storage and Disposal statement: [ ] Yes [X] No; if yes explain below:

7. Group **A**: Product Chemistry Data

Guideline No.	**Study Title**		**Data submitted**		**TRB's Assessment of Data**	**MRID Nos.**
			Yes	**No**		
830.1550	Product Identity & C position		X		A	49609001
830.1600	Description of materials used to produce the product		X		A	49609001
830.1650	Description of formulation process		X		A	49609001
830.1670	Discussion on the formation of impurities		X		A	49609001
830.1700	Preliminary analysis					
830.1750	Certified limits (158.350)	Standard certified limits	X			Revised Basic CSF (09-01-2015)
		Proposed Limits				
		Justification for wider limits				
830.1800	Enforcement analytical method		cited	X	A	49609002 49609003

8. Group **B:**

Guideline No.	**Study Title**	**Value or Qualitative Description**	**CITABB's Assessment of Data**	**MRID Nos.**
830.6303	Physical State	Oily Liquid	A	49609004
830.6314	Oxidation/reduction	Not expected to be oxidized nor reduced based on the chemical structures of the constituents. Therefore this data requirement is not triggered.	A	49609004
830.6315	Flammability	104°C	A	49609006 49609004
830.6316	Explodability	Does not contain any ingredients that are considered explodable.	NA	49609004
830.7000	pH	Not dispersible in water	NA	49609005
830.7100	Viscosity	About 5.9 cSt at 20°C	A	49609005 49609004
830.7300	Bulk Density	1.1 g/ml @ 20°C	A	49609005 49609005
830.6317	Storage stability*	The study is in progress, the results will be submitted on completion.	I	49609004
830.6320	Corrosion characteristics*	The study is in progress and the results will be submitted on completion.	I	49609004

A = Acceptance, N = Not Acceptable, G = Data Gap, W = Waiver request, NA = Not applicable, I = In progress.

* The accelerated studies (2 weeks at 54°C) can be submitted in lieu for one year.

C. CONCLUSIONS:

The CITAB has reviewed the proposed revised basic CSF and the supporting product chemistry data and has concluded:

1. The proposed revised basic formulation CSF (dated 09-01-2015) is acceptable.

2. The product chemistry data submitted corresponding to the guideline 830 series group A and group B are acceptable

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WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OFFICE OF PESTICIDE PROGRAMS
REGISTRATION DIVISION (7505P)

September 28, 2015

MEMORANDUM

Subject:	Name of Pesticide Product:	IMIDACLOPRID AND PYRIPROXYFEN SPOT-ON SOLUTION FOR CATS
	EPA Reg. No. /File Symbol:	83399-RA
	DP Barcode:	DP 428217
	Decision No.:	503583
	Action Code:	R315
	E-Sub#:	--
	PC Code:	129099 (Imidacloprid: 9.1%) 129032 (Pyriproxyfen: 0.46%)

From: Byron T. Backus, Ph.D., Toxicologist
CITAB
Registration Division (7505P)

Byron T. Backus
Sept. 28, 2015

Through: John Redden, M.S., Senior Risk Assessor
CITAB
Registration Division (7505P)

JCR

To: Rita Kumar/Venus Eagle RM 01
IVB3
Registration Division (7505P)

Registrant: CEVA ANIMAL HEALTH, LLC
8735 Rosehill Road
Lenexa, KS 66215

FORMULATION FROM LABEL:

Active Ingredient(s):		by wt.
129099 Imidacloprid		9.10%
129032 Pyriproxyfen		0.46%
Other Ingredient(s):		90.44%
	TOTAL	100.00%

ACTION REQUESTED: "CITAB/Companion animal team: Please provide a…full review of cited companion animal safety data to support registration of this cat spot-on product. This is an e-submission, and all the info is in Documentum: cover letter, data matrix, label, and CSF. Copies of cover letter and label dated 5/14/2015 are also attached."

BACKGROUND: The material available to CITAB includes a data matrix (dated April 17, 2015) with the following companion animal study citations: MRIDs 43679501, 43679502, 44157301, 44157302, 44179802, 45097001, 47924801, and 48085101. The proposed label indicates use on cats 8 weeks of age and older with three dose-weight ranges: 0.0078 fl. oz. or 0.23 mL for cats weighing 2 to 5 lbs; 0.014 fl. oz. or 0.4 mL for 5 to 9 lbs; and 0.027 fl. oz. or 0.8 mL for over 9 lbs.

COMMENTS AND RECOMMENDATIONS:

1. The density of this formulation is 1.100 g/mL (this information is from the acute oral LD_{50} study in MRID 49609007) so a dose of 0.23 mL on a 2 lb (0.907 kg) cat would be 0.28 g formulation/kg, or 0.025 g (25 mg) imidacloprid/kg. A dose of 0.4 mL on a 5 lb (2.268 kg) cat would be 0.202 g formulation/kg or 0.018 g (18 mg) imidacloprid/kg, and 0.8 mL on a 9 lb (4.08 kg) cat would be 0.216 g formulation/kg or 0.0196 g (19.6 mg) imidacloprid/kg. For pyriproxyfen (which has very low toxicity to mammalian species), 0.23 mL formulation on a 2 lb cat would be a dose of 1.28 mg pyriproxyfen/kg, 0.4 mL on a 5 lb cat would be 0.89 mg pyriproxyfen/kg, and 0.8 mL on a 9 lb cat would be 0.99 mg pyriproxyfen/kg.

2. The studies in MRID 43679501 and 43679502 were reviewed by HED (TXR 0011821; memorandum from Myron S. Ottley dated March 5, 1996) with the following comments:

   [For 43679501]: "A total of 4 males and 5 females in 3 groups (1-2/sex/group) were dermally exposed to Imidacloprid, 10% Spot-On formulation. Dose levels were 50 mg/kg/day x 1 day, and 50/mg/kg/day x 3 days. Controls received placebo (Formulation less active ingredient) at 50/mg/kg/day x 3 days. Animals then were observed for 14 days.

   "No major treatment related dermal, clinical signs, body weight effects or clinical chemistry changes were observed. Necropsy was not done due to lack of toxicosis. The study demonstrates that cats can tolerate 50 mg/kg without significant adverse reactions.

   "This acute dermal study is classified as Acceptable when combined with another study (see below). The number of animals/group is too small and not in keeping with general study practice. However, when data are combined with the companion study in the cat (MRID 43679502), the information is considered useful. This satisfies the requirements for a domestic animal study in the cat."

   [For 43679502]: "18 cats of various and mixed breed (3 or 4 males, 2 or 3 females per group of which 1 or 2 males/group and 1 or 2 females/group were 11 - 12 weeks old) were dermally exposed to Imidacloprid, 10% Spot-On at seven-day intervals for a total of eight treatments. Dose levels were 10 or 50 mg/kg. Controls received placebo (formulation less active ingredient) at 50/mg/kg.

"No major treatment related dermal, clinical signs, body weight effects or clinical chemistry/hematology were observed. Necropsy was not done due to lack of toxicosis. The study demonstrates that adult cats can tolerate up to 50 mg/kg of the active ingredient without significant reactions.

"This repeated dose dermal study satisfies the requirement for a Domestic Animal Safety study for topical use in adult cats and is classified as Acceptable."

It was the conclusion of the original reviewer that these two studies indicate adult cats can tolerate up to 50 mg/kg of the active ingredient, so they would (applying a 5X safety factor) support a dosage rate of 10 mg imidacloprid/kg. These studies then do not support the proposed maximum dosage rates for 83399-RA (0.23 mL on a 2 lb cat = 26 mg imidacloprid/kg; 0.4 mL on a 5 lb cat = 18 mg imidacloprid/kg; 0.8 mL on a 9 lb cat = 20 mg imidacloprid/kg).

3. The study in MRID 44157301 [Shmidl, J.; Arther, R. (1996) General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Six Week Old Kittens: Lab Project Number: 74746: TR-96F-004: 10332. Unpublished study prepared by Bayer Corp., DeSoto Research Facility. 41 p. Relates to L0000102] was reviewed by HED (TXR 0012322, memorandum from Virginia Dobozy dated September 24, 1997]. The following is from the executive summary:

   "In a domestic animal safety study (MRID # 44157301), six 6 week-old kittens/sex were treated with Advantage™ (9.1% imidacloprid) at 5X the recommended use rate (2.0 ml). Six kittens/sex were also treated with the vehicle control at the recommended use rate (0.4 ml). According to the study protocol, the animals were supposed to receive 8 treatments at weekly intervals. However, two males and two females in the imidacloprid-treated group died or were euthanized within 72 hours after the first treatment. On necropsy, the two females had suppurative cholangiohepatitis which was assumed to be due to an ascending bacterial infection in the liver. In addition, one female had mild diffuse hepatic lipidosis. There were no remarkable findings in the males… The study report concluded that the kittens were stressed from weaning and were not able to tolerate 5X the recommended use rate.

   "The study is considered unacceptable and cannot be upgraded. It was terminated prior to completion due to animal welfare considerations."

4. The study in MRID 44157302 [Shmidl, J.; Arther, R. (1996) General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Kittens Eight Weeks of Age: Lab Project Number: 74747: TR-96F-006: 10332. Unpublished study prepared by Bayer Corp., DeSoto Research Facility. 45 p. Relates to L0000102.] was reviewed by HED (TXR 0012322, memorandum from Virginia Dobozy dated September 24, 1997). The following is from the executive summary:

   "In a domestic animal safety study (MRID # 44157302), six 8 week-old kittens/sex were treated with Advantage™ (9.1% imidacloprid) at 5X the recommended use rate (2.0 ml) at weekly intervals for eight treatments. Six kittens/sex were treated with the vehicle control at the recommended use rate (0.4 ml) at weekly intervals for eight treatments. There was no evidence of treatment-related toxicity in clinical signs or clinical pathology parameters. All animals

gained weight during the study. It was demonstrated that 8 week-old kittens can tolerate a dose of 5X the recommended use rate.

"The study is considered acceptable and satisfies the draft guideline requirements (81-6) for a domestic animal safety study."

The initial body weights of the twelve 5X kittens are reported on page 8 of MRID 44157302; the 4 lowest weight males (0.73, 0.73, 0.83 and 0.84 kg) and 4 lowest weight females (0.82, 0.82, 0.85, 0.85 kg) had a mean weight of 0.81 kg . Since each was treated with 2.0 mL of a formulation containing 9.1% imidacloprid, they were each exposed to 207 mg imidacloprid which, divided by 0.81 kg, results in a mean of 256 mg/kg (207 mg ÷ 0.81 kg). **This study supports a dose rate of 256 mg imidacloprid/kg ÷ 5 = 51.1 mg imidacloprid/kg, which is greater than (and supports) the proposed maximum dosage rates for 83399-RA (0.23 mL on a 2 lb cat = 25 mg imidacloprid/kg; 0.4 mL on a 5 lb cat = 18 mg imidacloprid/kg; 0.8 mL on a 9 lb cat = 19.6 mg imidacloprid/kg).**

5. The study in MRID 45097001 [Abraham, A. (2000) Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot-on Formulation in the Target Species, Adult Cats: Lab Project Number: 75122. Unpublished study prepared by Bayer Corporation. 139 p. {OPPTS 870.7200}] was reviewed by TRB (TXR 5001582, memorandum from M. Hashim dated September 22, 2000). The following is excerpted from the executive summary:

"In a companion animal safety study (MRID 45097001), Advantage Plus® 9 and 18 for cats (Active Ingredients: 9.1% Imidacloprid w/w; 0.9% Pyriproyfen w/w) was topically applied at dose volumes of 2.0 ml for cats weighing less than or equal to 9 lbs, and 4.0 mL for cats weighing greater than 9 lbs (5 times the recommended doses) to groups of 6 male and 6 female cats, 7 months to one year of age. Controls were dosed with the vehicle at volumes of 2.0 mL for cats weighing less than or equal to 9 lbs and 4.0 ml for cats weighing greater than 9 lbs (5.6 times the volume of vehicle in the recommended doses). Animals were treated on (study) days 0, 7, 14, and 21.

"Treatment related clinical signs included transient salivation which ceased within 2 hours of treatment on day 0 (4 of 12 test animals and 1 of 12 vehicle control animals reported from licking the test material), and a rough hair coat appearance at the treatment site on all animals of both groups following treatment on days 14 and 21. None of the cats were observed salivating following the last 3 treatments. One animal from the test group had pruritis at one hour on day 21. There was vomiting by two cats in the test group on days 19 and 25, which did not occur in periods following the test (substance) applications. Vomiting may be associated with licking the test substance. This does not appear to be exposure related... There were no other treatment related effects on hematology, coagulation or clinical chemistry parameters. There were no treatment related effects on body weight or food consumption, and there were no signs of irritation at the application sites...

"Any clinical signs on the study showed no consistent toxicological response. This study is classified as **Acceptable /Guideline** for a companion animal safety study (OPPTS 870.7200) in cats. "

Individual body weights (in kg) are reported on p. 30 of MRID 45097001. Day -1 weights for the six group A (5X) females were 2.6, 2.7, 2.8, 3.1, 2.4, and 2.8 kg; weights for the six group A (5X) males were 4.1, 5.0, 4.9, 4.0, 3.9 and 3.8 lbs. From information on p. 33 all group A cats except for the two heaviest weight males received 2.0 mL test material on day 0; the two heaviest weight males each received 4.0 mL. On a bodyweight basis, individual dosage rates for the 6 females were 0.77, 0.74, 0.71, 0.65, 0.83 and 0.71 mL/kg; for the 6 males rates were 0.49, 0.80, 0.82, 0.50, 0.51 and 0.53 mL/kg. Taking the mean from the 4 highest values (0.83, 0.77, 0.74, 0.71 mL/kg) for the females and 4 highest values (0.82, 0.80, 0.53, 0.51 mL/kg) for males gives 0.71 mL/kg. The test material had (from p. 135 of MRID 45097001) a specific gravity of 1.097 and contained 9.1% imidacloprid, so the mean dosage in terms of this active was 71.3 mg imidacloprid/kg; dividing this value by 5 gives 14.3 mg imidacloprid/kg.

The study in MRID 45097001 then does not support the proposed maximum dosage rates for 83399-RA (0.23 mL on a 2 lb cat = 25 mg imidacloprid/kg; 0.4 mL on a 5 lb cat = 18 mg imidacloprid/kg; 0.8 mL on a 9 lb cat = 19.6 mg imidacloprid/kg).

6. The study in MRID 47924801 [Madsen, T. (2009) Evaluation of the General Safety of M880. Project Number: 152/141, S07648, 33714. Unpublished study prepared by Sinclair Research Center, Inc. 193 p.] was reviewed by TRB (TXR 5012077, memorandum dated April 15, 2010 from B. Backus). The following is excerpted from the executive summary:

"In a companion animal safety study (MRID 47924801), 5 groups, each containing 6 males and 6 females, of domestic shorthair kittens (54-57 days old on Day 0; Day -1 body weights: males: 0.691-1.012 kg; females: 0.555-0.935 kg; source: Liberty Research, Inc., Waverly, NY), were topically treated (on Day 0) with (Group 1): mineral oil at a total dose of 1.15 mL; (Group 2): 3X vehicle substance at a total dose of 0.63 mL; (Group 3): 5X vehicle substance at a total dose of 1.05 mL; (Group 4): 3X test substance at a total dose of 0.69 mL; and (Group 5): 5X dose test substance at a total dose of 1.15 mL...

"The groups and test materials they received (with amounts applied) are shown in the table below:

Group	Test Material Applied	Volume of each application	Cumulative amount applied on Day 0; also on Day 14
1	Mineral oil	1st app = 0.35 mL; 2nd & 3rd = 0.4 mL	1.15 mL
2	Vehicle of proposed formulation (no active ingredients) at 3X	3 applications @ 0.21 mL	0.63 mL
3	Vehicle of proposed formulation (no active ingredients) at 5X	3 applications @ 0.35 mL	1.05 mL
4	Proposed formulation (with active ingredients) at 3X	3 applications @ 0.23 mL	0.69 mL
5	Proposed formulation (with active ingredients) at 5x	1st app = 0.35 mL; 2nd & 3rd = 0.4 mL	1.15 mL

"All animals survived to the end of the study…

"It is concluded that the margin of safety in kittens administered topical application of the product formulation is at least 3X. Possible effects observed at 5X included lethargy in one male kitten following the second set of applications, and decreased body weight gains in both males and females in the period from day -1 to day 20. As noted in the current 870.7200 Guidelines: "Consideration will be given to products with less than a 5X margin of safety, depending on the severity of clinical signs of toxicity (e.g. transient, non-life-threatening signs)."

"This companion animal safety study in male and female domestic shorthair kittens is **Acceptable/Guideline** and **does satisfy** the guideline requirement for a companion animal safety study (OPPTS 870.7200) in 54-57 day (8 week) kittens."
Individual body weights for MRID 47924801 are reported on page 89 for males and page 90 for females. Individual day -1 bodyweights for group 5 (5X) males were 1.012, 0.881, 0.777, 0.857, 0.889 and 0.762 kg, and for group 5 (5X) females were 0.935, 0.786, 0.613, 0.746, 0.762 and 0.792 kg. The mean weight ± S.D. for the four least-weight males and four least-weight females is 0.773 ± 0.081 kg (1.704 ± 0.178 lbs). The test formulation density is reported (p. 18 of MRID 47924801) as 1.095. The minimum pyriproxyfen dosage for the 5X group on Day 0 is reported (p. 18 of MRID 47924801) as 5.848 mg/kg, and the minimum imidacloprid dosage is 110.744 mg/kg; since these values would be associated with the maximum weight kitten (1.012 kg) the [assayed?] percentages of actives can be calculated: formulation dosage was 1.15 mL x 1.095 g/mL = 1.259 g was applied to each kitten; 1.259 g ÷ 1.012 kg = 1.244 g/kg = 1244 mg/kg. The percentage of imidacloprid in the formulation was then 110.744 ÷ 1244.32 x 100% = 8.9% and the percentage of pyriproxyfen was 5.848 ÷ 1244.32 x 100% = 0.47% [According to the Certificate of Analysis on p. 68 of MRID 47924801 the percentage of imidacloprid was 9.1% and the percentage of pyriproxyfen was 0.46%].

Assuming the percentage of imidacloprid was 9.1% then the mean formulation dosage for the four least-weight males and four least-weight females was 1.259 g ÷ 0.773 kg = 1.629 g/kg, and the mean dosage of imidacloprid was 1.629 g/kg x 0.091 = 0.148 g/kg = 148 mg/kg. Dividing this by 5 gives 29.6 mg imidacloprid/kg for a 1X dose. The mean dosage of pyriproxyfen for these same kittens was 1.629 g/kg x 0.0047 = 7.66 mg/kg, and dividing this value by 5 gives 1.53 mg pyriproxyfen/kg for a 1X dose.

The study in MRID 47924801 then supports the proposed maximum dosage rates for 83399-RA (0.23 mL on a 2 lb cat = 25 mg imidacloprid/kg; 0.4 mL on a 5 lb cat = 18 mg imidacloprid/kg; 0.8 mL on a 9 lb cat = 19.6 mg imidacloprid/kg). For pyriproxyfen (which has very low toxicity to mammalian species), 0.23 mL formulation on a 2 lb cat would be a dose of 1.28 mg pyriproxyfen/kg, 0.4 mL on a 5 lb cat would be 0.89 mg pyriproxyfen/kg, and 0.8 mL on a 9 lb cat would be 0.99 mg pyriproxyfen/kg, all below the supported 1X value of 1.53 mg pyriproxyfen/kg.

7. The material in MRID 48085101 [Madsen, T. (2009) Imidacloprid + Pyriproxyfen: Addendum to Bayer Report No. 33714 (MRID 47924801) - Evaluation of the General Safety of M880. Project Number: 152/141, S07648, 33714. Unpublished study prepared by Sinclair Research Center, Inc. 9 p.] is an addendum to the report in MRID 47924801.

8. CITAB concludes that the citations to MRIDs 44157302 and/or 47924801 satisfy the companion animal safety data requirements (including minimum age of 8 weeks and the proposed maximum dosage rates of 0.23 mL on a 2 lb cat = 25 mg imidacloprid/kg; 0.4 mL on a 5 lb cat = 18 mg imidacloprid/kg; 0.8 mL on a 9 lb cat = 19.6 mg imidacloprid/kg) to support the registration of 83399-RA. MRID 47924801 also satisfies the proposed maximum dosage rates of pyriproxyfen (which has very low toxicity to mammalian species) since 0.23 mL formulation on a 2 lb cat is a dose of 1.28 mg pyriproxyfen/kg, 0.4 mL on a 5 lb cat is a dose of 0.89 mg pyriproxyfen/kg, and 0.8 mL on a 9 lb cat is a dose of 0.99 mg pyriproxyfen/kg, all below the supported 1X value of 1.53 mg pyriproxyfen/kg. **The citations in the data matrix satisfy the companion animal safety data requirements for the registration of 83399-RA.**

Pages 85-86 Claimed confidential by submitter

Screen

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

DP BARCODE No.: D428214; **FILE SYMBOL No.**: 83399-RA (screen); **PRODUCT NAME**: Imidacloprid & Pyriproxyfen Spot-On Solution for Cats; **DECISION No.**: 503583; **PC Code(s)**: 129099, 129032; **ACTION CODE**: R315; **FOOD Use**: No

DATE OUT: July 27, 2015

SUBJECT: Completeness check screening for end use product "Imidacloprid & Pyriproxyfen Spot-On Solution for Cats"

FROM: Shyam Mathur,
Product Chemistry Team Leader
CITAB / RD (7505P)

7/27/15

TO: Rita Kumar / Venus Eagle, RM 01
I-V Branch 3 / RD (7505P)

Company Name: CEVA Animal Health, LLC
Formulation Type: Insecticide
Active Ingredient(s): Imidacloprid (9.1%) and Pyriproxyfen (0.46%)
MRID Nos: 49609001 to 49609006

CONCLUSION:

Deficiencies: Yes
(if there are deficiencies they are indicated below each heading as Note 1, Note 2 Etc).

Group A: All required data submitted

Group B: All required data submitted

CSF: Basic CSF submitted (dated 04-15-2015)
Note 1: Basic CSF– Must be revised: In columns #11 of the CSF at least one name & address of the supplier for intentionally added inert ingredients must be listed. Alternate names & addresses of the suppliers must be provided on an attachment.

Note to PM: If the deficiencies are found in the screen results, please inform the registrant and bring back to author of this report the corrected deficiencies in response to 10 day letter, so that it can be attached to the original bean, if the data package is still in CITAB. New Bean is required in case the bean has been closed by CITAB. Thank you.

Kumar, Rita

From: Kumar, Rita
Sent: Monday, May 11, 2015 3:58 PM
To: Alicia Henk
Cc: Eagle, Venus
Subject: New dog and cat spot on applications 83399-RT and 83399-RA

Dear Alicia: I have not communicated with you in a while. Hope you are doing well and enjoying the spring weather.

I am doing a preliminary screen of these two spot-on applications, and have the following comments on the proposed labels:

1. Delete "[insert product name]", and add proposed product name on the front panel. This label must refer to the primary brand name.

2. Most of the brackets on the front panel statements and in optional marketing text are unnecessary or redundant, and make the label very confusing. Please simplify this label.

3. First Aid and Precautionary Statements are mandatory for both label and package insert. Delete the bracketed text from the two bulleted statements.

4. Delete the Optional text statement right below the two bulleted statements.

5. Delete the 3 optional text statements starting with: :Apply to cats.....". Only the sentence above with both minimum age and min weight are correct.

6. Delete brackets from the heading "[optional Marketing Text]".

7. The marketing text should be moved to end of the label. It should appear after the Precautionary statements and directions for use.

8. Delete "Fast Acting", or define it based on supporting efficacy data.

9. Under Directions for Use, the description of container (tube, via, applicator etc.) must match the picture. We suggest you use the term applicator, and delete other terms.

10. The statement regarding volume and pet weight needs to be clarified to reflect different volume and weight combination.

11. On the application form in column 6, indicate the product which was the basis of your proposed labeling and marketing text.

Please submit revised labels for further consideration of these applications. Since these are e-submissions, the revised labels must be uploaded to Documentum, therefore also be submitted on a CD thru front end with a hard copy of the cover letter explaining the changes, Please respond ASAP, so that the correct label can be sent for review. Thanks.

Regards,
Rita

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

May 19, 2015

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

ALICIA HENK
CEVA ANIMAL HEALTH, LLC
8735 ROSEHILL ROAD
LENEXA, KS 66215-

PRODUCT NAME: Imidacloprid & Pyriproxyfen Spot-On Solution for Cats
COMPANY NAME: CEVA ANIMAL HEALTH, LLC
OPP IDENTIFICATION NUMBER:
EPA FILE SYMBOL: 83399-RA
EPA RECEIPT DATE: 05/18/15

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 308-8045.

Sincerely,

Front End Processing Staff
Information Services Branch
Information Technology & Resources Management Division

Fee for Service {968646Q~

This package includes the following

- ◉ New Registration
- ○ Amendment

☐ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 1

Receipt No. S- 968646

EPA File Symbol/Reg. No. 83399-RA

Pin-Punch Date: 5/18/2015

☑ This item is NOT subject to FFS action.

Action Code:

Requested:

Granted:

Amount Due: $ _____

Parent/Child Decisions:

☐ Inert Cleared for Intended Use ☐ Uncleared Inert in Product

Reviewer: Jennifer Gaines Date: 5/19/15

Remarks:

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States **Environmental Protection Agency** Washington, DC 20460

☒ **Registration** ☐ **Amendment** ☐ **Other**

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
83399-NEW	Venus Eagle	☒ None ☐ Restricted
4. Company/Product (Name) Ceva Animal Health, LLC/Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs	5. PM #1	

5. Name and Address of Applicant (Include ZIP Code)

Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

☐ *Check if this is a new address*

6. **Expedited Review**. In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. Nos. 11556-150, 11556-151, 11556-152

Product Name Advantage II for cats

Section II

☐ Amendment - Explain below.
☒ Resubmission in response to Agency letter dated 05-11-2015
☐ Notification - Explain below.

☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Ceva Animal Health, LLC is re-submitting a new product label for Imidacloprid & Pyriproxyfen Spot-On Solution for Cats in response to an Agency email from Rita Kumar on May 11, 2015.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☒ No	☒ Yes ☐ No	☐ Yes ☒ No	☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag
***Certification must be submitted**	If "Yes" Unit Packaging wgt. / No. per Container: 0.014 fl oz (0.4 ml), 0.034 fl oz (1.0 ml), 0.085 fl oz (2.5 ml), 0.135 fl oz (4.0 ml) — 1,2,3,4,5,6, 12, 24, 50, 75, 100 vials	If "Yes" Package wgt. / No. per Container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	Various (see above)	☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☒ Other Printed box ☒ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Alicia Henk	Director, Development and Regulatory Affairs	(913) 754-7668

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature	3. Title
BY: Alicia Henk	Director, Development and Regulatory Affairs
4. Typed Name: Alicia Henk	5. Date: May 14, 2015

May 18, 2015

Venus Eagle, PM1
Office of Pesticide Programs (7505P) (REGFEE)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

RE: ***Re-Submission of Product Labels for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs (EPA File Symbol 83399-RT) and Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Cats (EPA File Symbol 83399-RA)***

Dear Ms. Eagle:

In response to the Agency's email from Rita Kumar dated May 11, 2015, Ceva Animal Health, LLC is submitting revised product labels for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs and Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Cats. In order to outline the changes to the label, the Agency's email is provided below with Ceva's responses typed in blue.

> On May 11, 2015, at 2:57 PM, Kumar, Rita <Kumar.Rita@epa.gov> wrote:
>
> Dear Alicia: I have not communicated with you in a while. Hope you are doing well and enjoying the spring weather.
>
> I am doing a preliminary screen of these two spot-on applications, and have the following comments on the proposed labels:
>
> 1. Delete "[insert product name]", and add proposed product name on the front panel. This label must refer to the primary brand name.
>
> A brand name was added to both products "CAH#".
>
> 2. Most of the brackets on the front panel statements and in optional marketing text are unnecessary or redundant, and make the label very confusing. Please simplify this label.
>
> We have removed the brackets on required statements and headings. We have also reduced the number of brackets in the optional marketing text section. However, some brackets remain on the label to indicate the text as optional.

3. First Aid and Precautionary Statements are mandatory for both label and package insert. Delete the bracketed text from the two bulleted statements.

We have combined the two statements into one simplified statement with no brackets, "See package insert for directions for use, precautionary statements and first aid".

4. Delete the Optional text statement right below the two bulleted statements.

This statement was removed. To explain the use of bracketing for optional text, we added a box on the first page with the heading "Master Label".

5. Delete the 3 optional text statements starting with: :Apply to cats.....". Only the sentence above with both minimum age and min weight are correct.

These statements have been removed.

6. Delete brackets from the heading "[optional Marketing Text]".

These brackets have been deleted.

7. The marketing text should be moved to end of the label. It should appear after the Precautionary statements and directions for use.

The optional marketing text has been moved to the end of the label.

8. Delete "Fast Acting", or define it based on supporting efficacy data.

All claims containing "fast acting" have been removed from the label.

9. Under Directions for Use, the description of container (tube, via, applicator etc.) must match the picture. We suggest you use the term applicator, and delete other terms.

The term 'applicator' is now consistently used within the directions for use. All other similar terms have been deleted.

10. The statement regarding volume and pet weight needs to be clarified to reflect different volume and weight combination.

The statements regarding volume and pet weights have been moved to the first page of the label under "Alternate Brand Names". We added a statement to indicate the product will be packaged in the listed weight ranges. The information is now concise to reflect only the weight range with corresponding product volume.

11. On the application form in column 6, indicate the product which was the basis of your proposed labeling and marketing text.

The application forms 8570-1 now contain information in column 6.

Please submit revised labels for further consideration of these applications. Since these are e-submissions, the revised labels must be uploaded to Documentum, therefore also be submitted on a CD thru front end with a hard copy of the cover letter explaining the changes. Please respond ASAP, so that the correct label can be sent for review. Thanks.

Regards,
Rita

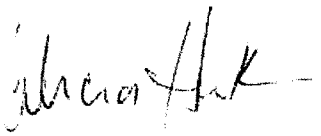
In addition to the Agency-requested changes, we have added the "How to Apply" section under the headings "Directions for Use", along with some additional formatting to clarify section breaks.

To support this submission, the following documents are provided on the enclosed CD:

- Form 8570-1 "Application for Pesticide" for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-on Solution for Dogs
- Form 8570-1 "Application for Pesticide" for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-on Solution for Cats
- Revised product label for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-on Solution for Dogs dated May 14, 2015
- Revised product label for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-on Solution for Cats dated May 14, 2015

If you have any questions regarding this submission, please contact me at 913-754-7668 or alicia.henk@ceva.com.

Sincerely,



Alicia Henk
Director, Development and Regulatory Affairs
Ceva Animal Health, LLC

Enclosures

Resubmission
5

May 18, 2015

Venus Eagle, PM1
Office of Pesticide Programs (7505P) (REGFEE)
U.S. Environmental Protection Agency
Document Processing Desk
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

RE: ***Re-Submission of Product Labels for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Dogs (EPA File Symbol 83399-RT) and Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution for Cats (EPA File Symbol 83399-RA)***

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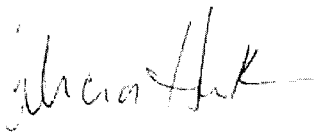

Alicia Henk
Director, Development and Regulatory Affairs
Ceva Animal Health, LLC

Enclosures

Claimed confidential by submitter

Kumar, Rita

From: Kumar, Rita
Sent: Monday, May 11, 2015 3:58 PM
To: Alicia Henk
Cc: Eagle, Venus
Subject: New dog and cat spot on applications 83399-RT and 83399-RA

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6. Delete brackets from the heading "[optional Marketing Text]".

7. The marketing text should be moved to end of the label. It should appear after the Precautionary statements and directions for use.

8. Delete "Fast Acting", or define it based on supporting efficacy data.

9. Under Directions for Use, the description of container (tube, via, applicator etc.) must match the picture. We suggest you use the term applicator, and delete other terms.

10. The statement regarding volume and pet weight needs to be clarified to reflect different volume and weight combination.

11. On the application form in column 6, indicate the product which was the basis of your proposed labeling and marketing text.

Please submit revised labels for further consideration of these applications. Since these are e-submissions, the revised labels must be uploaded to Documentum, therefore also be submitted on a CD thru front end with a hard copy of the cover letter explaining the changes, Please respond ASAP, so that the correct label can be sent for review. Thanks.

Regards,
Rita

21-Day Screen Completed by Contractor

21-Day Expires on 5-8-15

Jacket # 83399-RA
MRID# 496090

Content Screen: Recommend to Pass/Fail

11-3 Review: Pass/Fail/NA

Overall Status: Recommend to Pass/Fail

Transfer This Jacket to:

SHAUNTA HILL

PRIA 3 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

September 2012

21 Day Screen Start Date: 4-17-15

Experts In-Processing Signature: B.B. Date 4-22-15 Fee Paid: Yes ✓

Division management contacted on issues No_____ Yes_____ Date_____

EPA Reg. Number: 83399-RA	EPA Receipt Date: 4-17-15

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4)			X		
	a) All inerts, including fragrances, approved for the proposed uses (see Footnote A) non-food	**yes** X	**no**			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	**yes**	**no**			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) completed and signed (N/A if source is unregistered or applicant owns the technical)			X		
5	**Data Matrix** (EPA Form 8570-35) both internal and external copies (PR 98-5) completed and signed (N/A if 100% repack)			X		
	a) Selective Method (Fee category experts use)	**yes** X	**no**			
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label (Electronic labels on CD are encouraged and guidance is available)**			X		
7	**Is the data package consistent with PR Notice 86-5**			X		
8	**Notice of Filing included with petitions**					X

9	**If applicable for conventional applications, <u>reduced risk rationale</u>**			X
10	**<u>Required Data</u> and/or data waivers. See Footnote C.**			
	a) List study (or studies) not included with application			

Comments:

Documentation: Pass
Required forms are complete

Inerts: Pass
Approved for non-food use

II-3: Pass
MRID 496090 (e-sub)
MRID also associated w/ 83399-RT

Status: Pass
KC 4.30.2015

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses or have an application pending with the Agency. If an unapproved inert with no application pending with the Agency is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses or have an application pending with the Agency **even if a product is currently registered** by consulting the inert Web site and if the inert is not approved nor has an application pending with the Agency, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch.

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Provide the required information necessary to identify an inert approval application that is pending with the Agency; or

3. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

4. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R300 or R301), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

April 21, 2015

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OPP Decision Number: D-503583
EPA File Symbol or Registration Number: 83399-RA
Product Name: Imidacloprid & Pyriproxyfen Spot-On Solution for Cats
EPA Receipt Date: 17-Apr-2015
EPA Company Number: 83399
Company Name: CEVA ANIMAL HEALTH, LLC

ALICIA HENK
CEVA ANIMAL HEALTH, LLC
8735 ROSEHILL ROAD
LENEXA, KS 66215-

SUBJECT: Receipt of Registration Application Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your application and certification of payment. If you submitted data with this application, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: R315

NEW END-USE NON-FOOD ANIMAL PRODUCT WITH SUBMISSION OF TWO OR MORE TARGET ANIMAL SAFETY STUDIES;INCLUDES DATA AND/OR WAIVERS OF DATA FOR ONLY:;PRODUCT CHEMISTRY;ACUTE TOXICITY;PUBLIC HEALTH PEST EFFICACY);ANIMAL SAFETY STUDIES;CHILD RESISTANT PACKAGING;

No additional payment is due at this time.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 347-8961.

Sincerely,
Teresa Downs
Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service

{967252+~

This package includes the following

- ◉ New Registration
- ○ Amendment

☐ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ○ BPPD
- ◉ RD

Risk Mgr. 1

Receipt No. S-	967252
EPA File Symbol/Reg. No.	83399-RA
Pin-Punch Date:	4/17/2015

☐ This item is NOT subject to FFS action.

Action Code:

Requested: R315

Granted: R315

Amount Due: $ $400

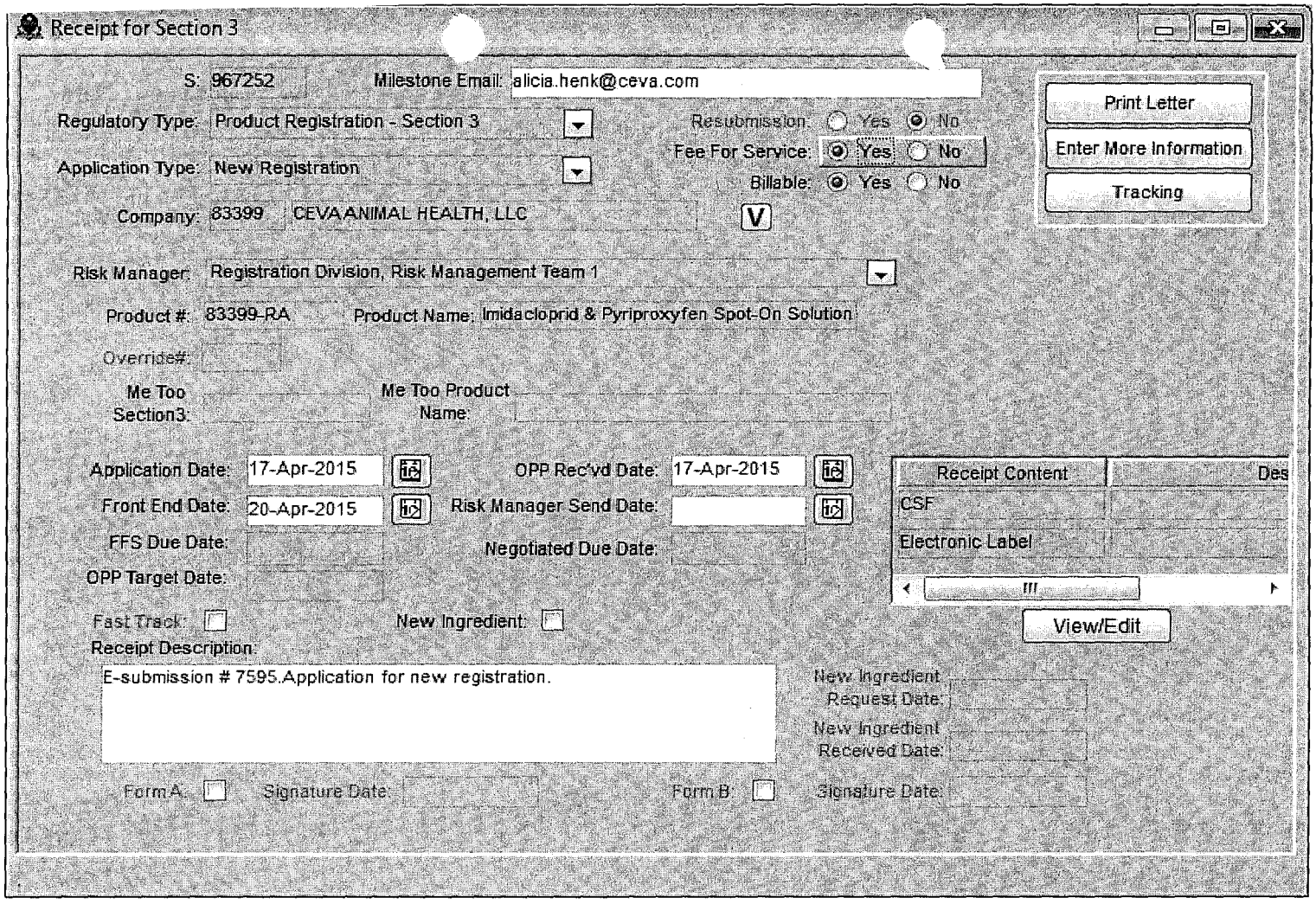
Parent/Child Decisions:

☒ Inert Cleared for Intended Use ☒ Uncleared Inert in Product

Reviewer: Jennifer Gaines Date: 4/21/15

Remarks:

e-Submission



Pay.gov

Receipt

Your payment is complete

Pay.gov Tracking ID: 25KRJCII
Agency Tracking ID: 74788230577
Form Name: Pesticide Registration Improvement Act - Prepayment
Application Name: PRIA Service Fees

Payment Information

Payment Type: Debit or credit card
Payment Amount: $8,400.00
Transaction Date: 04/16/2015 09:08:02 AM EDT
Payment Date: 04/16/2015
Registration Number:
Company Name: Ceva Animal Health, LLC
Company Number: 83399
Action Code: R315

Account Information

Card Holder Name: Tracey Bailes
Billing Address: 8735 Rosehill Rd
Billing Address 2: Suite 300
City: Lenexa
Country: United States
State/Province: KS
ZIP/Postal Code: 66215
Card Type: American Express
Card Number: **********2019

Email Confirmation Receipt

Confirmation Receipts have been emailed to:
katy.hernandez@ceva.com
alicia.henk@ceva.com

e-Submission

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

EPA United States **Environmental Protection Agency** Washington, DC 20460

☒ **Registration** ☐ **Amendment** ☐ **Other**

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number	2. EPA Product Manager	3. Proposed Classification
83399-NEW	Venus Eagle	☒ None ☐ Restricted
4. Company/Product (Name) Ceva Animal Health, LLC/Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	5. PM #1	

5. Name and Address of Applicant (Include ZIP Code)

Ceva Animal Health, LLC
8735 Rosehill Road
Lenexa, KS 66215

☐ *Check if this is a new address*

6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(I), my product is similar or identical in composition and labeling to:

EPA Reg. Nos. 1st product for labeling

Product Name

Section II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated XX-XX-XX
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated XX-XX-XX
☐ "Me Too" Application
☒ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Ceva Animal Health, LLC is submitting a new product registration application for Imidacloprid & Pyriproxyfen Spot-On Solution for Cats. Ceva Animal Health, LLC requests that the Agency review the end-use product registration as a 9 month PRIA timeframe under R315.

Section III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes* ☒ No	☒ Yes ☐ No	☐ Yes ☒ No	☐ Metal ☒ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) Plastic Bag
***Certification must be submitted**	If "Yes" Unit Packaging wgt. 0.0078 fl oz (0.23 ml) 0.014 fl oz (0.4 ml) 0.027 fl oz (0.8 ml) — No. per Container 1,2,3,4,5,6, 12, 24, 50, 75, 100 vials	If "Yes" Package wgt. — No. per Container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☒ Label ☐ Container	Various (see above)	☐ On Can ☒ On Labeling accompanying product

6. Manner in Which Label is Affixed to Product ☐ Lithograph ☒ Other Printed box ☒ Paper glued ☐ Stenciled

Section IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Alicia Henk	Director, Pharmaceutical Development and Regulatory Affairs	(913) 754-7668

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received **(Stamped)**

2. Signature	3. Title
BY: Alicia Henk	Director, Pharmaceutical Development and Regulatory Affairs
4. Typed Name: Alicia Henk	5. Date: April 17, 2015

Claimed confidential by submitter

Form approved. OMB No. 2070-0060, 2070-0057, 0-0107, 2070-0122, 2070-0164.

EPA

United States
Environmental Protection Agency
Washington, DC 20460

Formulator's Exemption Statement

(40 CFR 152.85)

Applicant's Name and Address	EPA File Symbol/Registration Number
Ceva Animal Health, LLC 8735 Rosehill Road Lenexa, KS 66215	83399-NEW
	Product Name Imidacloprid & Pyriproxyfen Spot-On Solution for Cats
	Date of Confidential Statement of Formula *(EPA Form 8570-4)* 04/15/2015

As an authorized representative of the applicant for registration of the product identified above, I certify that:

(1) This product contains the following active ingredient(s):

Imidacloprid
Pyriproxyfen

(2) Of these, each active ingredient listed in paragraph (4) is present solely as the result of the use of that active ingredient in the manufacturing, formulation or repackaging another product which contains that active ingredient which is registered under FIFRA Section 3, is purchased by us from another person and meets the requirements of 40 CFR section 158.50(e)(2) or (3).

(3) Indicate by checking (A) or (B) below which paragraph applies:

☑ (A) An accurate Confidential Statement of Formula *(EPA FORM 8570-4)* for the above identified product is attached to this statement. That formula statement indicates, by company name, registration number, and product name, the source of the active ingredient(s) listed in paragraph (1).

OR

☐ (B) The Confidential Statement of Formula (CSF)(EPA Form 8570-4) referenced above and on file with the EPA is complete, current, an accurate and contains the information required on the current CSF.

(4) The following active ingredients in this product qualify for the formulator's exemption.

Source

Active Ingredient	Product Name	Registration Number
Imidacloprid Pyriproxyfen	[redacted]	

Signature	Name and Title	Date
	Alicia Henk Director, Development and Regulatory Affairs	04/17/2015

EPA Form 8570-27 (Rev. 06-2004)

Copy 1 – EPA
Copy 2 - Applicant copy

Product ingredient source information may be entitled to confidential treatment

Submission

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
WASHINGTON, D.C. 20460

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215	EPA Registration Number/File Symbol 83399-NEW
Active Ingredient(s) and/or representative test compound(s) Imidacloprid, Pyriproxyfen	Date 04/17/2015
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Indoor non-food	Product Name Imidacloprid & Pyriproxyfen Spot-On Solution for Ca

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).	☑ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☑ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

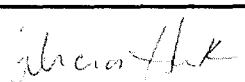
I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses .

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (I) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
	04/17/2015	Alicia Henk, Director, Development & Reg. Affairs

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version.

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

RA

Date: April 17, 2015		**EPA Reg No./File Symbol:** 83399-NEW	Page 1 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215		**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	
Ingredients: Imidacloprid, Pyriproxyfen			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Product Chemistry					
830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1750	Group A Product Chemistry for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609001	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution	49609002	Ceva Animal Health, LLC	OWN	
830.1800	Assay Determination of Imidacloprid and Pyriproxyfen in Imidacloprid 9.1% (w/w) and Pyriproxyfen 0.46% (w/w) Spot-On Solution: Analytical Method Validation Report	49609003		OWN	
830.6302, 830.6303, 830.6304, 830.6313, 830.6314, 830.6315, 830.6316, 830.6319, 830.6321, 830.7000, 830.7100, 830.7300. 830.7520	Summary of Group B Product Chemistry and Waivers for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609004	Ceva Animal Health, LLC	OWN	
830.6302, 830.6303, 830.6304, 830.7100, 830.7300	Physical and Chemical Characteristics: Color, Physical State, Odor, Viscosity, and Density for Ceva Animal Health's Imidacloprid & Pyriproxyfen Spot-On Solution	49609005	Ceva Animal Health, LLC	OWN	
830.6315	Flashpoint for Ceva Animal Health's Imidacloprid Spot-On Solution, Imidacloprid & Pyriproxyfen Spot-On Solution, and Imidacloprid & Permethrin Spot-On Solution	49609006	Ceva Animal Health, LLC	OWN	
Toxicology Data Requirements					
870.1100	Acute Oral Toxicity Study of Imidacloprid Pyriproxyfen Spot On Solution in Sprague-Dawley Rats	49609007	Ceva Animal Health, LLC	OWN	
870.1200	Acute Dermal Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096905	Bayer Animal Health	OLD	
870.1300	Acute Four-Hour Inhalation Toxicity Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096906	Bayer Animal Health	OLD	
870.2400	Acute Eye Irritation Test of Imidacloprid/Pyriproxyfen Spot On Solution in New Zealand Albino Rabbits	49609008	Ceva Animal Health, LLC	OWN	
Signature	**Name and Title** Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC			**Date** April 17, 2015	

Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: April 17, 2015		**EPA Reg No./File Symbol**: 83399-NEW	Page 2 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215		**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	
Ingredients: Imidacloprid, Pyriproxyfen			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.2500	Primary Dermal Irritation Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096908	Bayer Animal Health	OLD	
870.2600	Dermal Sensitization Study with Imidacloprid (9.1%)/Pyriproxyfen (0.9%) Spot On in Rats	45096909	Bayer Animal Health	OLD	
870.7200	Acute Toxicity Evaluation for Dermal Treatment of Cats with Imidacloprid (Bay t 7391) Spot-On: Lab Project Number: TR-94D-010: 74579. Unpublished study prepared by Miles Inc. Animal Health DeSoto Research Facility. 19 p	43679501	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Bay t 7391) Spot-On On Cats: Lab Project Number: TR-95F-006: 74591. Unpublished study prepared by Bayer Corp. DeSoto Research Facility. 41 p	43679502	Bayer Animal Health	OLD	
870.2600	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Six Week Old Kittens: Lab Project Number: 74746: TR-96F-004: 10332. Unpublished study prepared by Bayer Corp., DeSoto Research Facility. 41 p. Relates to L0000102.	44157301	Bayer Animal Health	OLD	
870.7200	General Safety Evaluation for Topical Use of Imidacloprid (Advantage) Spot-On on Kittens Eight Weeks of Age: Lab Project Number: 74747: TR-96F-006: 10332. Unpublished study prepared by Bayer Corp., DeSoto Research Facility. 45 p. Relates to L0000102.	44157302	Bayer Animal Health	OLD	
870.7200	Acute Oral Toxicity Evaluation of Imidacloprid (Advantage) in Cats: Lab Project Number: TR-96F-011: 74769: J:USERS\LINDA\NOREPORT\JAS0173.RP. Unpublished study prepared by Bayer Corp., Animal Health. 10 p.	44179802	Bayer Animal Health	OLD	
870.7200	Evaluation of the General Safety of M880	47924801	Bayer Animal Health	PAY	
870.7200	Imidacloprid + Pyriproxyfen: Addendum to Bayer Report No. 33714 (MRID 47924801) - Evaluation of the General Safety of M880	48085101	Bayer Animal Health	PAY	
870.7200	Evaluation of the General Safety of 9.1% Imidacloprid with 0.9% Pyriproxyfen Spot-on Formulation in the Target Species, Adult Cats	45097001	Bayer Animal Health	OLD	
Product Performance Test Guidelines					
810.3300	Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Cats: Lab Project Number: MIC 194: 74571. Unpublished study prepared by Agresearch Consultants, Inc. 32 p.	43679503	Bayer Animal Health	OLD	

Signature	**Name and Title**	**Date**
	Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	April 17, 2015

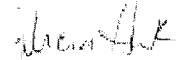
Form Approved OMB Nos. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

DATA MATRIX

Date: April 17, 2015		**EPA Reg No./File Symbol:** 83399-NEW	Page 3 of 3
Applicant's/Registrant's Name & Address Ceva Animal Health, LLC, 8735 Rosehill Road, Lenexa, KS 66215		**Product:** Imidacloprid & Pyriproxyfen Spot-On Solution for Cats	
Ingredients: Imidacloprid, Pyriproxyfen			

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
810.3300	Efficacy Evaluation of Bay t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Fleas on Cats: Lab Project Number: PD-7391-95F-004: 74581. Unpublished study prepared by Professional Laboratory and Research Services, Inc. (PLRS). 46 p.	43679504	Bayer Animal Health	OLD	
810.3300	Efficacy Evaluation of BAY t 7391 (Imidacloprid) 10% Solution Applied Dermally for Control of Adult Fleas and Flea Eggs on Cats: Lab Project Number: BH036/95: 74634: 95REPORT/AUSTRALI.DOC. Unpublished study prepared by Bayer Australia Ltd. 33 p.	43794101	Bayer Animal Health	OLD	
810.3300	Controlled Field Trials on the Efficacy and Tolerance of a Spot-On Formulation of Imidacloprid (BAY NTN 33893) 10% for Control of the Cat Flea (C. felis) in Domestic Cats: Lab Project Number: HVS 95-01: 74635: 95REPORT/74635.DOC. Unpublished study prepared by Institute of Parasitology, Hannover Vet School. 7 p.	43794102	Bayer Animal Health	OLD	
810.3300	Comparative Evaluation of How Quickly Advantage and Frontline (Fipronil) Top Spot Kill Fleas on Dogs: (final Report)	44256901	Bayer Animal Health	OLD	
810.3300	Imidacloprid Topical Formulation: Larvicidal Effect Against Ctenocephalides felis in the Surroundings of Treated Dogs	44256902	Bayer Animal Health	OLD	
810.3300	Evaluation of the Effects of Shampooing or Water Immersion on the Initial and Residual Efficacy of Advantage for Flea Control on Dogs	44256903	Bayer Animal Health	OLD	
810.3300	Nylar 50 (percent) Concentrate: Product Performance/Efficacy Reports. Unpublished study prepared by McLaughlin Gormley King. 79 p.	45086801	McLaughlin Gormley King Company	OLD	

Signature	**Name and Title**	**Date**
	Alicia Henk, Director, Pharmaceutical Development and Regulatory Affairs, Ceva Animal Health, LLC	April 17, 2015

Pages 117-125 Confidential Statement of Formula may be entitled to confidential treatment